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CEREBRAL SCLEROSIS.

BY ALFRED W. CAMPBELL, M.D.EDIN.

From the Pathological Laboratory at Rainhill Asylum, Lancashire.

With 19 *Figures.*

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INTRODUCTION.

DERIVED from the Greek word σκληρός, the equivalent of the Latin *durus*, the term sclerosis denotes induration. It has been applied, perhaps too freely and with inadequate regard to pathogenesis, to a number of conditions of the brain having increased firmness, local or general, as a common character.

In this paper I propose to consider all the known forms of sclerosis, touching lightly on varieties familiarised to us by frequent occurrence, and giving details of rarer kinds.

Cerebral sclerosis is nearly always a secondary condition, reparatory or hyperplastic, and following some disturbance or destruction of normal constituents. Only in rare instances is it a pure katabiotic product, and even then suspicion of the operation of a primary factor cannot be wholly suppressed.

Viewed from the standpoint of histology, sclerosis is almost invariably synonymous with gliosis; also, it is almost of necessity associated with alterations in the more fundamental constituents of the central nervous apparatus, the nerve cells and their appurtenances, the stations and conductors of nervous impulses. It is seen in its simplest and purest form as an outcome of secondary degeneration of one of the known tracts of medullated nerve fibres, and is then reparatory. It will be well here to glance at the sequence of events which leads up to this particular form of sclerosis. The process begins in necrotic swelling and disintegration of the myelin and possibly of other constituents of the medullated nerve fibres. Then ensue important secondary changes in the nutritive apparatus and supporting tissue of the part. As a mechanical result of the swelling of the fibres, the vascular and lymphatic channels are interfered with and conditions favourable to the emigration of lymphocytes and leucocytes set up; with this is associated an enlargement[1] of the supposed fixed neuroglia residents, brought about by one or both of two causes, defective metabolism from impeded blood and lymph circulation, and irritation by or reaction to the toxic products of myelinic decay (cholin and allied substances). The next stage is one of absorption of the diseased and disintegrated nerve fibres. What the agents are here it is impossible to say, but some would give force to the supposed scavenger function of enlarged neuroglia cells, while others would credit the phagocytic capacity of

[1] It is a moot point whether the enlarged neuroglia cells we see in such cases are changed residents or formative cells recently derived from the blood-vessels or lymphatics. In my opinion the latter is the case.

altered leucocytes and lymphocytes, and probably both are subservient, co-operating in the absorption of diseased products, and in the connection of such products to the lymph and blood channels now relieved of their primary embarrassment. In the final stage the place of the medullated nerve fibres is taken by a poorly vascularised mass of neuroglia or connective tissue cells and their processes, in the midst of which thick-walled vessels, some of them newly formed, ramify. I have seen it stated that cerebral sclerosis is not accompanied by shrinkage, but this does not apply to all forms, and certainly not to the simple form of sclerosis just used as an example. If proof on the point be needed, it is afforded by the alterations in form of the spinal cord seen in cases of tabes dorsalis and in cases of descending degeneration affecting the motor tract.

The principles seen in this simple instance of the manner in which sclerosis plays a reparatory *rôle*, apply to many varieties of cerebral induration; that which we find so often around old-standing foci of softening and of hæmorrhage, that which is the outcome of impaired nutrition and which affects individual gyri (local microgyria), that resulting from agenesia and affecting whole lobes or even hemispheres, and many other forms, can be grouped as essentially of the same nature. In all an overgrowth of neuroglial constituents is a common character representing Nature's effort to make complementary amends for a deficiency, destructive or developmental, of nerve cells and nerve fibres.

Other forms of sclerosis have a mixed pathogenesis. In causing the initial necrosis of fundamental constituents and the superimposed reparative or repellent proliferation of neuroglia, *an irritant is the primary factor*. This may act locally or generally. The induration observed in general paralysis of the insane, a disease in which we assume for granted the circulation of noxious blood, instances the general condition, the sclerosis round an imprisoned foreign body the local.

Lastly, there are rare forms of sclerosis in which the principal constituent is not neuroglia, but some other element or structure. Thus, I shall have occasion to describe a

condition in which hyperplasia of ganglionic nerve cells has been found accountable for the induration, and in this class "colloid sclerosis," with its vascular alteration, must needs be included. These, however, are borderland cases, and it is an open question whether they should not be called outright tumours or new formations.

Chapter 1.—General Remarks on the Neuroglia.

Some observations on the neuroglia must be introduced here, because it is the most prominent tissue in nearly all the conditions of which I shall write. Since, however, it is a tissue whose attributes have been discussed at length by many able writers, of whom the late Professor Weigert, von Lenhossek, and Storch, in Germany, and Dr. Ford Robertson in our own country, may be specially mentioned, it is proper that my remarks shall be shorn of detail and, though flavoured with criticism, made pertinent to the histogenesis and pathology of the condition in hand.

First, in order that the tissue may be considered in its relation to sclerosis, we must look at the varieties of neuroglia which have been recognised in the central nervous system.

While others have generally classified varieties of glial elements according to their morphological and structural peculiarities, I have always found it more convenient, paying regard to their chemical affinities, to arrange them according to their behaviour in the presence of different dyes and histological reagents. In doing this, I have avoided pitfalls into which others seemed to have plunged.

§ 1.—*The Neuroglia in Sections Stained by the Method of Bevan Lewis.*

As my earliest acquaintance with the neuroglia was formed from an examination of sections prepared by the fresh method of Dr. Bevan Lewis, I will begin by commenting on the revelations of this process. And I will here take the opportunity of expressing the belief that if others, in particular continental workers, had been more generous in their recognition of this method, past controversies re-

garding the structure of the neuroglia might have been considerably abbreviated.

So many years have elapsed since Dr. Bevan Lewis gave us his earlier publications, that many others in this country have made themselves familiar with his process and confirmed his observation that, in frozen sections of the fresh brain stained with "blue black" and some other aniline dyes, two kinds of glia cell are displayed, one small, the other large.

The smaller elements vary from 6 to 9 μ in diameter, and have a spheroidal, intensely-stained nucleus, surrounded by an extremely delicate protoplasmic investment apparently devoid of processes. They appear in three situations, irregularly distributed throughout the nerve fibre framework, in regular series around nerve cells, and in more or less regular succession along the course of the blood-vessels.

The larger elements are usually 13 μ in diameter, and are further distinguishable from the smaller by a preponderance of protoplasm over nucleus, by relatively pallid staining of the nucleus, by their flask-like form, and by showing numerous delicate radiating processes, one of which, stouter than the rest and attached to the wall of a neighbouring capillary, is known as the vascular process. In the normal brain such cells occur chiefly in the outermost layer of the cortex and in the white or medullary projection of a convolution. They bear a constant relation to the blood-vessels of the cortex. These are the cells described by Deiters in the year 1865; by many they are called after him "Deiters' cells"; but "scavenger cells," on account of their supposed phagocytic function, and "large spider cells," are other names which have been applied. We shall have frequent occasion to return to these cells, because as a factor in the production of cerebral sclerosis and as a feature in other morbid conditions of the cortex they possess great importance.

§ 2.—*The Neuroglia in Sections Impregnated with Salts of Silver.*

The service rendered to the neuro-histologist by Golgi when he elaborated his well-known process cannot be over-

estimated. For the embryologist the method has no equal; with its aid all the beautiful work of Golgi, His, Capobianco, and Fragnito, and others, on the development of the neuroglia has been performed. Similarly, the ordinary histologist will vouch that with this process, or one of the many modifications which have been recommended, a clearer demonstration of, at any rate, the external form of the neuroglial element is obtained than by any other method.

The display in a silvered preparation of the normal cortex is very different from that in a fresh section stained with aniline blue black; in fact, there is some difficulty in correlating the appearances. The elements seen may be briefly described as follows: (1) Cells with short (hence the German name "Kurzstrahler"), thick, mossy, or feathery branching processes roughly coated with the deposit of the silver derivative, one of which is a vascular process. These cells, admirably fitting the designation "spider cell," have the same distribution as the larger elements to be seen in fresh sections, and, although the silver coat alters their general appearance, there is no doubt that the two are identical. (2) Cells with a smaller body, from which numerous delicate, long (hence the German name "Langstrahler"), and clearly-defined processes radiate. A vascular attachment can be found sometimes, but not always. The term "stellate" applies well to the shape of these cells. The white matter is again their elective site, and they are never far removed from a blood-vessel. (3) The third variety of cell was, I think, first described by Retzius, and occurs only in the plexiform layer (Ramón y Cajal) of the cortex, immediately beneath the pia mater. They seem to hang down from vessels in the pia mater, to which they are attached by several processes, including the vascular process; and from the opposite or central end of the body there springs a pencil of branching, delicate, and occasionally moniliform processes.

It is commonly stated that the three varieties of cells whose characters I have just described are all transition forms of one element. This is a statement to which I am inclined to subscribe my belief. In this connection the

character they have in common of growing in direct contact with a blood-vessel is most important. For, when we take notice of the point that they all have a different environment, one deposited in the loose substance of the cortex, another in the dense plexus of fibres in the white substance, and the third next the surface of the brain; when, also, we recollect how variable in its chemical reaction to silver salts is protoplasm in general, the statement gains additional justification.

Unfortunately, I cannot leave the silver method without expressing a word of regret. Excellent as the methods of Golgi, Cox, and Ramón y Cajal are as aids to the embryologist and the normal histologist, their fickleness of action condemns them in the eyes of the histopathologist, and I have found them of little value in my examination of sclerosed tissues.

§ 3.—*The Neuroglia in Sections Stained by the Methyl Violet Method of Weigert.*

We appeal next to a method which has received a high measure of praise, because of all methods it alone can pretend to be selective in action. Much faulty reasoning, however, seems attributable to overdriving this selective virtue. Simple constitutional principles appear to have been neglected. It has been forgotten that almost all tissues are chemically and structurally complex, and that to meet this combination there necessarily must be selection within selection. Take the nerve cell as an instance. Step by step we have perfected our knowledge of its structure by discovering that one dye or one means of impregnation selects and displays the cell envelope, another the tigroid bodies, another the neurofibrils, and so on. Accordingly, we find in practice that not one but many methods of staining have to be gone through before we obtain a satisfactory demonstration of the structure and condition of any nerve cells. And surely the same applies to the neuroglia.

I have made this explanation preparatory to saying that I share the opinion of those who refuse to entertain the statement of the late Professor Weigert that the nucleus and the fibrils in the neuroglia cell are chemically different

to those investigating the condition of diseased tissues, because, for some unknown reason, it is uncertain in its results, and the risk of spoiling tissue when the supply is limited is a deterrent to its employment; but, as we all know, these imperfections were an admitted source of regret to the illustrious professor at the time of his death.

§ 4.—*The Neuroglia Cell in Sections Stained by the Platinum Method of Ford Robertson.*

Dr. Ford Robertson insists strongly that the neuroglia is not composed of one element, as is generally believed, but of two kinds of cells, of which "the origin, morphology, and behaviour in morbid conditions are entirely distinct." This hypothesis is based on the revelations of a specially-devised method of impregnation with platinum. The elements which Dr. Ford Robertson has discovered, and for which he proposes the name "mesoglia," are blackened by platinum, while the ordinary neuroglia cell is only darkened. They are small cells, with scanty perinuclear protoplasm and three to six delicate processes which tend to branch dichotomously. These processes, compared with those of the ordinary neuroglia cell, are short and sometimes varicose; they form no vascular attachment, indeed, special relation with any other structure has not been determined. Though first observed in the brain of the dog, such cells have been found in man also, and they are said to occur throughout the central nervous system. Some may think that Dr. Ford Robertson's evidence is scarcely strong enough to clinch the supposed mesoblastic origin of these cells; even so, and granted that more information is required, their discovery alone is an important addition to our knowledge of the glia.

I have now exhausted the list of stock methods for the display of glial elements, though in practice other stains and reagents are of contributory service; for instance, I have frequently obtained a beautiful view of the neuroglia as it appears in the white substance of the brain in sections primarily stained for neurofibrils by the method of Bielschowsky; and rubin, as recommended by Kultschitzky,

and morphologically separate. The statement is one which has been much discussed, and, although the preponderance of authority is unfavourable, it still finds many adherents. Those, however, who have stained and studied the neuroglia by various methods, and in conditions of health and disease, are forced to conclude that the supposition of the late Frankfort professor rested on a faulty basis. Without denying that the fibrils and the nucleus of the neuroglia cell differ chemically, they will rest their argument on the point that the neuroglia cell, like many other cells, is composed of envelope, nucleus, hyaloplasm, and spongioplasm. Each constituent requires special treatment for its display, and the last is peculiar in that it harbours fibrils, which extend along the processes and have a special affinity for methyl violet. The case, therefore, is one of limited selection. The method affords an exquisite display of the framework of the cell, but fails to show the covering; and I think that this may explain why Weigert held that the neuroglia cell had no vascular attachment, for we have reasons for assuming that this particular process is composed of non-fibrillar protoplasm.

And now a word on a question which has arisen out of the controversy to which I have just alluded. Can the neuroglia fibre live independently of the cell body? Possibly, but that existence is qualified by certain conditions. It appears that the neuroglia cell in the fully-developed form has a definite period of life, that there is a cycle in its history, that in its earliest form it is a nucleated mass of structureless protoplasm, that the formation of its contained fibres is a comparatively late phase, and that in the stage of devolution the nucleus and investing protoplasm disappears, leaving nothing but the fibrils behind. Unless some transition of this nature takes place, it is impossible to explain many forms of sclerosis in which the method of Weigert, and several other methods, display a dense fretwork free from nuclei of any description and composed exclusively of delicate fibrils.

As with the method of Golgi, so with the method of Weigert; as it stands at present it does not commend itself

vessels. In short, our information leads us to suppose that the neuroglia is descended from both epiblast and mesoblast.

And now, referring the reader desirous of further details on the early development of the neuroglia to the monographs of Golgi, His, Capobianco and Fragnito, and Ford Robertson, we can pass to a matter of more immediate interest, the history of the neuroglia in the later periods of life.

In this connection we seek information more precise and comprehensive than that already supplied on the series of tissue changes in the developed brain which end in sclerosis. And when we analyse our requirements we find that they nearly all revolve round one question, whether this sclerosis is brought about by a proliferation and hyperplasia of pre-existing elements or by the formation of new elements? This question I shall try and answer.

Thinking that profit might accrue from closely watching the sequence of events in the tissues surrounding cerebral lesions, both those arising in nature and those of artificial production, I carried out a special series of observations. For the artificial lesion I took a number of white rats, plunged a red-hot needle into the brain of each, and then killed the animals and examined the lesion after periods varying between one and twenty-one days. The brains of a series of cases of cerebral softening in the human subject, which I have collected and placed in the museum at Rainhill Asylum, afforded rich material for examining the changes in a natural lesion; more than this, the latter study safeguarded me against the objection that my results might have been invalidated by structural differences between the human brain and the brain of the rat.

In narrating the conclusions drawn from this examination, it will be convenient to take up in turn the varieties of cells met with and trace their life history. This will embrace an account of cells which I will classify as follows:—

(1) Large mononuclear phagocytes.

(2) Polymorphonuclear leucocytes and compound granular cells.

(3) Eosinophile cells.

(4) Lymphocytes or lymphoid cells.

Mallory's hæmatoxylin, and several of the carmine preparations now falling into disuse, may prove convenient in helping us out of difficulties, but none of these stains reveals any elements not demonstrable by the principal methods, and therefore may be dismissed.

§ 5.—*Summary Enumeration of Neuroglial Elements.*

(1) The large neuroglia cells of the fresh method of Dr. Bevan Lewis, corresponding to the spider cells of the method of Golgi, and also revealed by the method of Weigert. Synonyms: large spider cell, scavenger cell (Bevan Lewis), Kurzstrahler (Lenhossek and other German authorities).

(2) The stellate cell of the method of Golgi, also revealed by the method of Weigert, and possibly representing a phase in the development of No. 1. Synonyms: small spider cell, Langstrahler.

(3) The cell next the surface of the cortex, displayed by the method of Golgi, possibly representing a form taken by No. 1 in an unusual environment. Synonym: glia cell of Retzius.

(4) The smaller cell of the fresh method of Dr. Bevan Lewis, sometimes spoken of as a nucleus of the neuroglia.

(5) The mesoglia cell of Dr. Ford Robertson.

Chapter 2.—Development and Growth of the Neuroglia.

In the year 1885 Golgi told us that he had seen epithelial cells in the chick's spinal cord which he thought gave origin to the neuroglia; these cells lined the neural canal, and from processes which they sent out to the pia mater the neuroglial element seemed to grow.

Since this opening speculation, many others have devoted attention to the subject, and, extending Golgi's observations, they have obtained evidence which suggests that other neuroglial elements may spring from the primitive epithelial cells of the central canal as well as from cells of the neural canal, and others, again, from mesodermic elements, penetrating the nervous system along with the embryonic blood-

§ 1.—*The Large Mononuclear Phagocytes.*

By the large mononucleated phagocytes (the designation is borrowed from Beattie) I mean cells which are, without doubt, the most important constituents in the conditions with which I am dealing. They are considerably larger than a leucocyte; their nucleus is large, crescentric, or reniform, and usually eccentric; it often touches the margin of the cell, and is supplied with chromatin, scanty and sometimes knobbed beneath the nuclear membrane. A nucleolus is almost always recognisable; the body protoplasm is scanty, with most dyes it remains homogeneous, but with Unna's alkaline methylene blue it stains darkly and shows some fine granules. These are the characters in the first stage of development, and I think it will not be denied that such cells are identical with cells described by many other observers in different inflammatory conditions, and called variously *large mononucleated leucocytes* (Metchnikoff), *infiltration cells* (von Marschalko), *pseudo-plasma cells* (Hodara), &c. Let us follow the history of these cells. In the early stage of a lesion, be it a hæmorrhage, a softening, or an artificial destruction, they are not at all prominent; if, however, we search along the vessel walls, particularly along the walls of vessels lying just without the focus of destruction, we may find what I take to be the originals of these cells. In the first state they appear to consist of nucleus alone; at any rate, the investing ring of protoplasm is extremely delicate, and it is at this stage that we get a hint as to their origin, for they are seen in such intimate connection with the walls of capillaries that it seems certain they are derived either from the endothelium lining these vessels or from contiguous lymphatics. It is not clear how they multiply, but, although I have not seen mitosis, I believe they divide by this method. Detached from the vessel wall, I imagine they next migrate to surrounding tissues, and their further development belongs to another stage.

In a similar lesion about six days old the conditions are changed; difficult to find previously, the cells in question now seem abundant, but this apparent increase in number is due in no small measure to an increase in size; they

approach the mature state. The nucleus remains as it was, but is so eccentric that it often looks as if it were on the point of breaking away from the cell. The scanty ring of body protoplasm is supplanted by a copious, pale-stained, homogeneous, or finely-stained mass, from the serrated edges of which many coarse processes extend, and it is significant that one of these processes establishes a direct connection with the nearest capillary or arteriole. Next, after a few days, the cell becomes reduced in size and the protoplasm of the processes condensed and converted into deeply-stained fibrils.[1]

Cells of this character may be recognised for weeks and even months after the preliminary disturbance, and may be studied conveniently in the tissues surrounding a patch of "yellow softening," where they are present in great abundance. In such material I have observed changes in these cells which have an important bearing on the histogenesis of sclerosis. Thus, as the cells grow older they lose their distended globose figure, and their processes become larger and more attenuated. And in this stage one is struck by the resemblance they bear to the larger neuroglia cells of the normal brain; indeed, the appearances afford proof, almost positive, that the commoner forms of sclerosis are brought about by the deposition and metamorphosis of new elements, and not by the proliferation of pre-existent cells; also they strengthen our belief in the statement of Fragnito and Capobianco, that in the course of development the ingrowing blood-vessel is an important channel for the convection and introduction of the nuclei from which the neuroglia grows.

Passing on to the final stage in the history of these cells, displayed, for example, in the walls of an excavation resulting from old softening, the case is one of still further shrinkage. As an outcome of contraction and failure of nutrition from autochthonous vascular obliteration, the body

[1] When making these observations I had forgotten for the time being that Dr. Watson had made a study, wanting nothing in exactitude, of the developing neuroglia in the brain of the juvenile general paralytic. It is satisfactory to find, however, that what is written above is quite in harmony with Dr. Watson's fuller and more precise account. (*Archives of Neurol. London County Asylums*, ii., 1903.)

and nucleus of the cell either disappear or become changed into small, round, deeply-stained nuclei; the processes gain independence, but remain as attenuated and filamentous fibrils contributing to the formation of a network of great density. Touching the nuclear remnants, it is possible that they represent what are often called the nuclei of the neuroglia, that is, deeply-stained, circular, or oval nuclei; and, as it is absurd to think of a nucleus without function, it is possible that these bodies persist to exert some influence in the maintenance of adjacent neuroglia fibres.

Concerning the function of the cells, the life history of which has just been given, I have no hesitation in agreeing with Beattie and others in saying that they possess phagocytic properties, because in the swollen state it is common to see particles of blood pigment, the products of myelinic disintegration, and even nucleated bodies (leucocytes or lymphocytes) included in the cell body. I do not think, however, that they play such an important *rôle* in the absorption and removal of diseased and foreign matter as do the leucocytes; the part they fill in a later phase, that of binding and strengthening the zone of substance bordering the destroyed area, is of greater importance. Then, speaking of the function of neuroglia cells in general, it is in accordance with these data to suppose that in certain phases a cell may act, as Bevan Lewis suggests, as a scavenger, while in others it may serve as connective tissue, and in the latter capacity coincidently it might fulfil the part of an isolator (Eurich, &c.). That these cells are directly connected with the lymphatic system is for me difficult to believe, but that in an indirect manner they serve as drains for lymphatic fluid is readily credible, and in this capacity it seems of little moment that the vascular process should be solid instead of canaliculated, a point out of which some have made capital in criticising this hypothesis. Here the siphonic action of a piece of string or worsted is a physical truth to be held in view.

Satisfied that the cell described is the most important element in the process of repair as it affects the brain substance, only a short account of other cells met with is called for.

§ 2.—*The Polymorphonuclear Leucocytes and Compound Granular Cells.*

In all artificially-produced and many natural lesions, in early and in late stages of the process, these cells, lying collected within and in the neighbourhood of obstructed blood-vessels, are prominent objects. So often are they choked with masses of blood pigment, altered proteids and detritus, that there can be no doubt they are more active agents in the removal of products of degeneration and disease than the large mononucleated cells; moreover, in this case they re-exhibit the phagocytic properties they are known to show in those conditions in which micro-organisms are the principal objects for removal.

The constant presence of these polymorphonuclear leucocytes in the cases of cerebral lesion in hand has naturally excited the suspicion that one might be a transition form of the other; more than this the frequent occurrence of collections of kindred leucocytes (compound granular cells, as they are sometimes called) along the blood-vessels in patches of disseminated sclerosis and slowly-progressing myelitis, appears to favour the possibility that these are the originals of glial or connective tissue cells. I have therefore taken considerable pains to arrive at the truth on these points, and I can say now that, while my specimens provide abundant illustrations of swelling, fragmentation, and dissolution of these elements, all proof of their persistence and metamorphosis into the large mononucleated astrocyte is absent.

§ 3.—*Eosinophile Cells.*

The coarsely-granular eosinophile cells of the blood seem to play no part of importance in the process of repair.

§ 4.—*Lymphocytes or Lymphoid Cells.*

The plasma cells of von Marschalko have been attracting attention lately, because it has been stated that they are pathognomonic of general paralysis of the insane, and, as they are present in some of the conditions of which I shall treat,

they must be noticed. According to von Marschalko, they are derived from the lymphocytes or, as he calls them, the lymphoid cells of the blood, and they are described as having scanty, non-granular protoplasm, and an eccentric oval nucleus showing several chromatin granules and a nucleolus.

These cells resemble in many particulars the large mononuclear phagocytes in their earliest state of development, and whether they are derived from the endothelium of blood-vessels or from lymphocytes, it is my belief that they are identical with these phagocytes.

Chapter 3.—Tuberose Sclerosis.

Synonyms.—Sclérose tubéreuse ou hypertrophique du cerveau (Bourneville). Multiple tuberöse Sklerose des Gehirns. Hypertrophic nodular gliosis (Sailer). Neurogliosis gangliocellularis diffusa (Hartdegen and Neurath). Anoia (Sherlock).

First described by Bourneville in the year 1880, tuberose sclerosis is one of the most extraordinary diseases with which the neuro-pathologist has to deal. Not only are the potato-like (hence the name tuberose) masses of sclerosis in the brain unique in kind, but the accompanying affections of parts related neither to the brain nor to one another are as singular as they are difficult to explain.

Sailer found twenty-eight cases reported in medical literature. I have not been so fortunate; still, I have read accounts of twenty; and on running over the salient clinical features, the first point which struck me, one which I desire specially to emphasise, is that no less than seventeen suffered from idiocy or imbecility, and that, even in the remaining three, congenital mental weakness could not be excluded. This complication, remarkable in itself, suggests an intrauterine origin for the cerebral disease which underlies it.

Convulsions, identical with those of ordinary ideopathic epilepsy, form a second clinical manifestation, and although unmentioned in some reports, seem to have been invariably present in all the best recorded cases.

The frequent and, I believe, constant occurrence of the

peculiar and rare skin affection, adenoma sebaceum,[1] is a third sign, which, taken in conjunction with those just mentioned, as well as the youth of the patient, may lead to a diagnosis of the disease during life. The age limit for the occurrence of this disease is 25 years.

Great patches of indurated cortex, projecting nodules in the ventricles of the brain, and fibroid subcapsular tumours in the kidney, complete the extraordinary combination.

While most writers make no attempt to explain the remarkable complex of diseases, the pathology of the cerebral changes has been the subject of much speculation. Taking a retrospect we find that the view meeting most support—it is the only one which brings all the somatic changes into line—is that we have to deal with some obscure developmental anomaly of the nervous system. And touching the time of life at which this arises, it is probable that the process is in activity at birth, because Hartdegen has recorded a case in a newly-born infant. It appears also that although the germs may be sown earlier, they cannot be active before about the seventh month of intrauterine life, the month when the plan of the sulci and gyri is laid down. We are entitled to this assumption because we have learned from our studies of porencephaly that when the destructive lesion peculiar to that disease occurs prior to the seventh month, the effort on the part of the growing cerebrum to make good the deficiency results in distortion and a characteristic fan-shaped and bizarre arrangement of sulci and gyri around the lesion. When, on the other hand, the lesion occurs after the seventh month the gyri and sulci surrounding the destroyed part can all be identified and the arrangement is orderly. Now, in tuberose sclerosis, in spite of the deposit of great masses of fibroid

[1] Adenoma sebaceum is a congenital affection having a predilection for the skin covering the bridge of the nose and the naso-labial folds; it is said to consist of hypertrophy of the sebaceous glands, which appear as minute, shotty nodules, lifting the epidermis and projecting above the general surface level. Pringle gives a good and succinct account of the disease in "Quain's Dictionary of Medicine" (3rd edition, London, 1902), and mentions the interesting facts that the observed cases have generally been afflicted with mental disease, and that other congenital diseases of the skin, such as warts, moles, nævi, and fibromata, have commonly co-existed.

material all over the brain, there is no disturbance of external morphology. Therefore, knowing the distorting effects of cicatrisation, we cannot suppose that the sclerotic process assumes activity before the time I have mentioned.

Other views on the genesis of the condition can be soon dismissed. Fürstner and Stühlinger, in assuming that a leptomeningitis arising in intrauterine life or early youth is the cause of a chronic gliosis, not only take an unwarranted liberty, but fail to account for the other somatic changes.

Koch's explanation seems to rest solely on a coincidence. In his case, thickening and adhesion of the pia mater beneath an old fracture of the parietal bone betrayed a difficult labour, and the application of forceps, which he was led to regard as a cause of the sclerosis; but we have had so many cases of tuberous sclerosis not so complicated that this suggestion cannot be entertained.

The fourth view, that of Scarpatetti, puts the onus of the disease on syphilis in the parents, "as a result of which multiple hæmorrhages affect the brain of the offspring at an important period of intrauterine development and call forth an extremely chronic form of reactive inflammation." This, again, fails to explain the invariable coexistence of the changes in the skin and kidneys; moreover, the constancy of the syphilitic taint has yet to be proved.

A microscopic examination seems to have been carried out in most of the recorded cases, and all observers agree in stating that the brain masses are composed of a dense network of proliferated neuroglia, choking and destroying the nerve-cell and nerve-fibre elements; only three writers, Sailer, Hartdegen and Neurath, mention the presence of scattered but exquisitely formed giant or ganglionic nerve cells. Such cells are most interesting constituents of the masses; they occur in my specimen, and, since in a preliminary examination I overlooked them, I am inclined to think that others may have done the same. More than this, I think that they are constantly present. Accordingly, Hartdegen and Neurath are misleading when they call the disease "glioma gangliocellulare," for, although this name

correctly conveys the histology of the condition, when unqualified it creates the false impression that it is a disease distinct from tuberose sclerosis. Besides, we must not forget that there is another altogether different form of cerebral sclerosis associated with the presence of ganglionic nerve cells.

I will now proceed with the account of my case.

Clinical History.

The patient, a male, was admitted to Rainhill Asylum at the age of 6 years, and died therein at the age of 16. He came from a workhouse, and, unfortunately, no information regarding his family history could be obtained. Examination, on admission, revealed no sensory, motor or nutritional abnormality, but adenoma sebaceum was noticed affecting the skin covering the bridge of the nose and the naso-labial folds. Though congenital syphilis could not be excluded, the teeth were in good condition, and there were no outward indications of this disease. His mental state was one of idiocy. When spoken to he lifted his head, but his expression proved that he did not comprehend language; nor could he use it. He would pick up objects and handle them in an aimless way, but did not resent their removal, apparently forgetting that he had just had them in his possession. He was ill-tempered, restless, given to wandering about in an objectless manner, and to distorting his body and making grimaces.

He suffered from epilepsy, and this is the sequence of events observed in a fit occurring soon after admission. The opening cry was succeeded by conjugate deviation of the eyes to the right, and by dextriversion of the hand. The spasm was more marked in, and almost confined to, the muscles of the left side. When recovering, he placed his hands to his mouth and moved his jaws as if chewing at a bone. There was no expulsion of fæces or urine.

Beyond learning to understand and carry out simple instructions, the boy made no mental progress; physically, on the other hand, he developed normally, with this exception, his cranium failed to expand in proportion to his body growth, and left him distinctly microcephalic. He continued to suffer from epilepsy, averaging five fits a month, a number which dropped to one a month during the last year of life. Five months before death he was treated in the infirmary for an obscure attack of

pyrexia. This was transitory, and, at the time, regarded as trivial, but when he returned to the care of his usual attendant it was noticed not only that he was more apathetic and irritable than before, but that he was quite blind. (The necropsy proved that this attack was due to occlusion of both posterior cerebral arteries.) After this he gradually failed, and death was ascribed to exhaustion from epilepsy.

It is noteworthy that the record of the case contains no reference whatever to tremor, to paresis, or to any similar manifestation which we might expect to be associated with the cerebral sclerosis.

Anatomical Examination.

The Brain.—The brain was below the average in size and weight, the encephalon scaled 1,210 grammes, the right hemisphere 476 grammes, the left hemisphere 500 grammes, both unstripped, and the cerebellum with the pons and medulla 157 grammes. The occipital lobes were reduced in size by bilateral adventitious softening, to be described presently; but there was no lobar deformity or disparity which we could set down to defective development, and, in accordance with my introductory remarks, the disposition of gyri and sulci was free from striking peculiarity. (Fig. 1.)

The sclerosed masses characterising the disease did not obtrude, indeed, at first glance the surface appeared healthy; on closer inspection, however, numerous patches were observed, twelve or more in each hemisphere, some circular, others irregular in form, ranging between 1·5 and 5 cm. in diameter, and universally distributed, although chiefly occupying the frontal lobes of both sides, and the parieto-temporal region of the right side. These patches were characterised by an extraordinary firmness—they were little softer than costal cartilage—by a paler tint and a more granular aspect than surrounding parts, by projecting slightly above the surface level and by being coated with pia, not adherent, but poorer in vessels and more delicate than the rest. It was noticed, further, that some of these patches presented slight central umbilication, that the proximal wall or lip of bordering sulci was bulged so as to operculate the

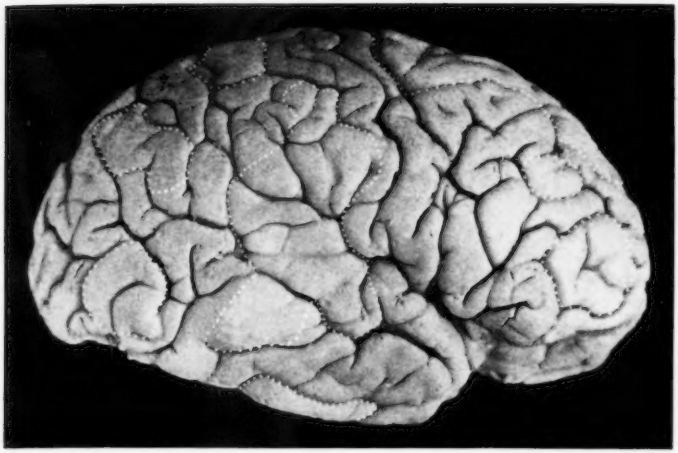

FIG. 1.

Photograph of the outer surface of the right cerebral hemisphere in the author's case of tuberose sclerosis. The distribution of the sclerosis is indicated by the dotted lines. The patches cause no disturbance in the plan of the convolutions.

FIG. 2.

Microphotograph of a giant nerve-cell from one of the sclerosed patches. × 400. In the original specimen, stained by Bielschowsky's method neuro-fibrils can be plainly seen.

opposite distal wall (a manifestation of cortical hypertrophy), and that in most cases the outline was sharp, though occasionally the passage from cartilaginous firmness to normal consistence was gradual. On section, the cortex was manifestly increased in depth, and the depth of invasion of the white substance was not in proportion to the surface extent; indeed, I think it may be correctly said that the sclerosis was mainly confined to the cortex and that only the immediately subjacent white substance was affected. This applied, at any rate, to most of the deposits; therefore, in regard to morphology, while the term "tuberose" aptly expressed the outward appearance of the masses it did not fit the sectional view.

So much for the cortical deposits. I have now to describe another variety of neoplasm seen on opening the lateral ventricles, which were dilated. These growths were of quite a different character, small (about the size of a split pea), white and very hard, they projected above the surface and were distributed along the lines of the venules, coursing over the basal nuclei and draining into the main vein of the corpus striatum. Others do not seem to have noticed this relation to the venules, but it is important and will be referred to again in discussing the histogenesis of the disease. One deposit, larger than the rest and situated beneath the ependyma lining the anterior horn of the lateral ventricle, appeared at first sight to be of different nature, but microscopic examination proved that this was not so. Subependymal growths of this description have been repeatedly observed in "tuberose sclerosis," and their occurrence quite away from the surface of the brain suggests that the original germs of the disease are sown elsewhere in addition to the cortex.

The occipital shrinkage previously alluded to was the result of bilateral occlusion by thrombosis of the posterior cerebral artery; the subsequent softening comprised the "area striata" (the area presenting the line of Gennari) and a portion of the subjacent lingual lobule. The affected parts were yellowish-brown and much contracted. Seeking a cause for the thrombosis, we found sclerosed masses

(*b*) *Nerve cells.*—It might be supposed that nerve cells could not exist in the presence of such profound tissue metamorphosis; they do, however, and their nature and condition demands careful consideration. There is, of course, a fall in numerical representation, and it varies in relation to the march of the sclerosis, being greatest in the most severely sclerosed parts, but nowhere is the cell destruction complete. It appears that the first cells to go are those of small size, namely, cells in the first, second, and fourth (stellate) layers. Some larger pyramids and some fusiform cells remain to the end, but while they retain their erect position and their apical and basal processes, their bodies become attenuated and their reaction to stains changes. With Nissl's method the protoplasm stains deeply and homogeneously, and Bielschowsky's process displays no neurofibrils.

Mention of neurofibrils leads on to another most extraordinary feature of this disease, one to which I have already briefly alluded; it is that the sclerosis is associated with the deposit or evolution of aberrant nerve cells, cells which in point of size and shape are akin to the large multipolar "motor" cells of the normal precentral cortex, and for which, therefore, the designation "giant" or "ganglion" cell is appropriate. (Fig. 2.) Such cells are not numerous, only one or two may be discovered in a section measuring two square centimetres; they affect no particular cortical level, at times being found near the surface, at others in the depths, and occasionally even in the subjacent white substance; they may occur in groups, but it is commoner to find them solitary. Structurally they are peculiar, inasmuch as the method of Nissl displays a protoplasm devoid of all chromophilic elements, non-pigmented, and practically homogeneous, while the method of Bielschowsky proves the persistence of neurofibrils.

It is a point of interest and importance that cells of this description have been recognised in all the masses examined, and, whether growing in the frontal, central, parietal, temporal, or occipital region, they have presented a uniform appearance.

attacking the cortex in the stem of each calcarine fissure; they bulged into the fissures, and their pressure must have directly induced stasis and coagulation in the arteries. Such a bilateral softening is rare, and explained the patient's sudden blindness.

The cerebellum, pons, medulla, cranial nerves, spinal cord, and all remaining structures pertaining to the nervous system, appeared normal.

In the trunk the condition of the kidneys attracted attention. In each quite a dozen firm, round, white growths, 1 to 5 mm. in diameter, were seen projecting above the surface level; they were implanted in the cortex, but not deeply, as some came away with the capsule when it was stripped; they did not occur in the medullary substance, and otherwise the kidneys were healthy. Similar growths have been constantly found in the kidneys in other cases.[1]

In the left lung we found two wedge-shaped patches, solid and uniformly gray in colour, which we took for resolving infarcts, but there was no zone of congestion around and no heart disease[2] to account for them, so that our diagnosis may have been at fault.

The remaining organs were free from special disease.

Microscopic Examination.

(1) *Sclerosed Cortex.*

(*a*) *Nerve fibres.*—Sections which I have treated by the method of Wolters-Kulschitzky show profound want of fibres. There is no trace of a zonal layer, delicate fibrils are scattered about in the supraradiary layer, a line of Baillarger is barely discernible, the interradiary spaces are swept almost bare, only a few fibres remain to mark the position of the radiations of Meynert, and even these seem to be bereft of their myelinic investment. Such changes are more pronounced in the centre than at the periphery of the masses.

[1] In Sailer's case a large "adeno-sarcoma" of the kidney was found, but I am inclined to doubt the correctness of the microscopic diagnosis.

[2] Ugolotti found a "fibro-myoma" in the heart muscle.

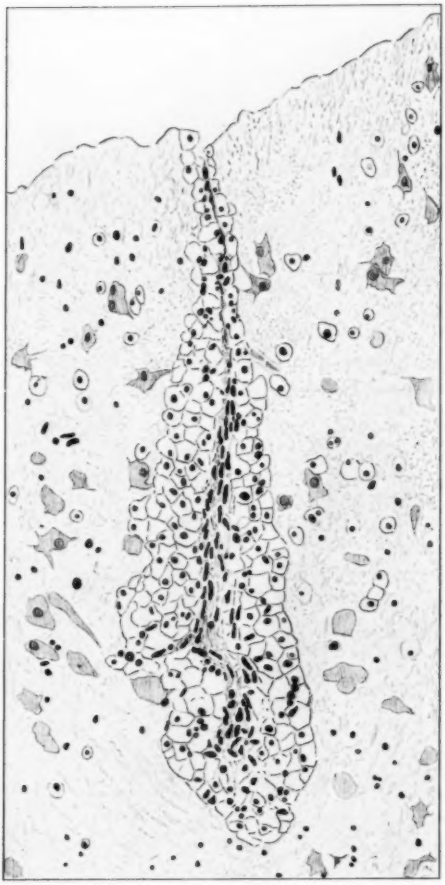

FIG. 3.

Tuberose Sclerosis.

A camera lucida drawing of one of the remarkable gland-like structures described in the text; it leads down from the surface, is tubular, ends in a blind alveolar expansion, and is lined with columnar cells.

Young neuroglia cells are to be observed in the neighbourhood. (Shaded in the figure.)

Beilschowsky's stain. Magnification × 200.

(*c*) *Matrix.*—Examining a piece of tissue from the centre of one of these indurated areas, we find a matrix composed of a dense network of indefinite structure, a tissue showing neither nuclei nor distinct fibres, and one which is probably the outcome of a past neuroglial proliferation. Active neuroglia cells (methods of Weigert and Bielschowsky and staining with rubin) vary in abundance in different parts of the deposit and in different deposits; few are found in the central portions of the masses, nor are bodies which we can call nuclei of the neuroglia present in this situation. At the lateral edge of the masses, however, particularly around the gland-like structures to be described presently, and all along the surface of the cortex, I have found cells of glial nature in great abundance. Some of these are shown in the accompanying drawings (fig. 3), and attention is invited to their peculiar character, especially their great size, their succulent bodies, and their coarse processes.

(*d*) *Blood-vessels.*—Nowhere are the blood-vessels numerous, and those seen have normal, thin walls.

(*e*) *Other structures.*—I have now to describe some structures which have an important bearing on the histogenesis of the masses, structures so peculiar in themselves, and so foreign to the cortex cerebri, indeed, to any part of the nervous system, that I consider it necessary to illustrate one (fig. 3). They are found at the peripheral or growing edge of the deposit, and may be described as tubular glands, leading from the surface inwards for a distance of about 1 mm., and ending in blind alveolar expansions. Not having studied them in serial sections, I cannot tell definitely whether they branch, but I think they do. The lining cells are of columnar form, pallid, and finely granular, and they contain a well-stained nucleus. The basal membrane is indistinct, but "centro-acinar" cells (Langerhans) are present in the lumen of the tube from end to end. These "glands"—so I suppose we must call them—are not numerous, for although I saw one or more ducts cut transversely in almost every section, not often did I find the mouth and whole length of a gland as here represented. But while "glands," such as I have described, are only found

in what I take to be the growing part of the deposits, at the periphery, indications are not wanting that the remainder has been permeated at some time by similar structures, for dotted about in all situations are circular or oval cells 10 to 15 μ in diameter, without processes, finely granular, and with a deeply-stained nucleus 2 to 3 μ in diameter. These I take to be glandular vestigia, not only because they resemble gland epithelium cells more than anything else, but because their number and arrangement varies in different parts of each deposit; in parts where the cortex is of cartilaginous hardness, and the process apparently most advanced, such cells, though present, are not numerous; in other growths which are softer, and apparently of more recent origin, they occur in abundance; moreover, reminiscent of the tabular arrangement, several cells are occasionally seen in line and in apposition.

(2) *The Subependymal Growths.*

The subependymal tumours have not the same microscopic characters as those in the cortex. A single layer of ependymal epithelial cells coats the surface. Immediately below, separating the surface from the main growth, is a shallow layer, composed of densely interwoven delicate fibrils, and containing short lines and groups of ependymal cells. In this layer runs the vein which the growths follow; it looks distended, but the wall is healthy, and so likewise are the accompanying arteries.

The basis of the growth is composed of a more or less open network of coarse fibrous tissue (much too coarse to be called glial tissue), and a remarkable appearance is imparted by an abundance of corpora arenacea, like those seen in a choroid plexus which has undergone calcareous degeneration. Small vessels are numerous, and, since they nearly all have thick calcereous walls, and since where they are most numerous, so also are the corpora arenacea, I think there can be no doubt, as has been inferred by previous observers in other diseases, that there is a developmental relation between the two.

Of nerve cells there are none; indeed, in all the small

ependymal growths nucleated cells of any description are scarce. The larger ependymal growth, however, which I have especially referred to, contains, and in fact is almost entirely composed, of cells so remarkable that I figure them (fig. 4). They are elongated and fusiform, and have homogeneous protoplasm and one to three oval nuclei. It is difficult to arrive at a conclusion concerning the nature of these cells, but I hazard the opinion that they are of endothelial origin, and this on account of their resemblance to cells seen in growths regarded as endotheliomata. The difference in appearance between this and the smaller ependymal growths does not necessarily signify a different origin. I take it that the smaller growths are the older, and that they have undergone fibrous and calcareous degenerative changes.

(3) *The Tumours in the Kidneys.*

On microscopic examination these tumours are found to be sharply circumscribed, but not encapsulated. They retain no renal structure, and are composed for the most part of long nucleated cells, smaller, but otherwise not unlike those seen in the larger subependymal cerebral growth. Blood-vessels are numerous, and many show thickening of the adventitia.

Reflecting on the remarkable complex of changes, naked eye and microscopic, furnished by this disease, interest at once turns on the question of histogenesis. And, in considering the origin of the various growths, weight attaches to the determination of the nature and source of several products revealed by the microscope; first, the acinoid structures, which I seem to have been the first to recognise, in the masses of sclerosis on the surface of the brain; secondly, the giant nerve cells finding a place in the same masses; thirdly, the cells composing the intraventricular and the renal growths; and, lastly, the components of the cutaneous deposits.

In taking a retrospect of the propositions which have been advanced to account for the cerebral growths, I

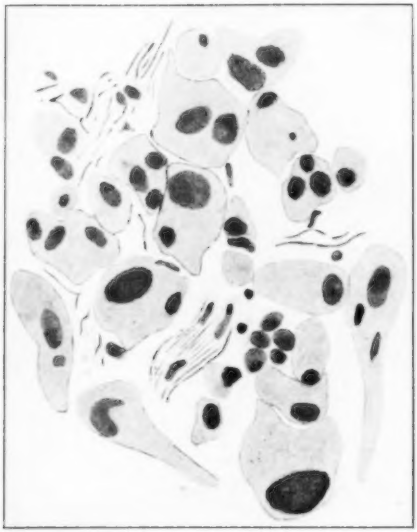

FIG. 4.

Tuberose Sclerosis.

A drawing of some of the endothelioid cells in one of the subependymal ventricular growths.

Silver method of Bielschowsky. × 500.

indicated the certainty that the morbid process, whatever it be, must be active during intrauterine life, although not before the seventh month. It is likely, therefore, that we have to deal with some aberration or disturbance of development, and along this line we will pursue our inquiry.

The preliminary point as to which of the three embryonic tissues, epiblast, mesoblast, or hypoblast, is selected for affection we can soon dismiss, not because the settlement of the point is unimportant, but because the tissue giving rise to one of the organs in which we are interested, the kidney, is undetermined. We know that the nervous system and the skin spring from epiblast, but which layer provides the kidney is still unsettled. Hence we cannot group the affected organs and parts into one category, stating that they are of common embryonic origin. Nor is it necessary, for, in describing the histology of the renal and the intraventricular growths, I insisted that the principal cell constitutents of both had characters reminiscent of cells occurring in endothelial neoplasms; likewise in the case of the growths lodged in the cerebral cortex, I pointed out that gland-like endothelial expansions were present, and were probably the cause of the neuroglial proliferation. This structural correlation is of great importance, in fact, it affords a clue to the solution of our problem, because if my primary assumption that all these growths have an endothelial basis is correct, it only remains to find the source of the endothelial elements. We are not without a guide. I think that the lining cells of blood vessels—probably veins—or of perivascular lymphatics will supply our wants, and such a source, in explaining the occurrence of kindred growths in various organs and parts, related to one another neither spacially nor developmentally, will overcome one serious difficulty.

While advancing my arguments for the vascular origin of these endothelial elements, it will be convenient to mention a few points which annul a possible alternative proposition, that they arise from endothelium-clad membranes. In the first place, a relation between the growths in the cortex cerebri and the arachnoid endothelium

might be suggested. Of this I will say merely, there is no evidence: there is no thickening, no adhesion, nothing to favour such a relation. On the other hand, the growths in question arise in a part which is particularly rich in arterioles, venules and perivascular lymph spaces; moreover, when the specific constituents to which I have drawn attention, the gland-like structures, are seen on longitudinal section, the arrangement of cells lining the mouth and the neck is singularly reminiscent of what one has often seen in cerebral perivascular channels.

Secondly, the intraventricular growths might be referred to a proliferation of cells of the ependymal lining, but, as I have shown, there is no indication of ependymal hyperplasia, and, on the other hand, there is clear and suggestive evidence of an intimate relation with subependymal venules.

Thirdly, the peritoneum might be thought to give rise to the renal growths, but this is in opposition to the observation that growths occur on the dorsal surface of the kidney, well away from the peritoneum, while, in support of my contention, the close relation of these growths with the venæ stellatæ cannot be gainsaid.

Lastly, in the case of the cutaneous tumours the endothelium of sebaceous glands is to be considered. At the same time, it must be remembered that these growths affect the most vascular part of the face, also, that in some histological reports written by dermatologists, the "nævoid" character of the growths is emphasised.

Therefore I feel justified in asserting that while the relation of the various growths to some endothelium-bearing structure is suggestive, that relation is neither so intimate nor so convincing as it is to the blood-vessels.

If, then, it be allowed that the endothelial cells forming the basis of these deposits is derived from blood or lymph channels, what is the process of evolution, and why should it be confined with such remarkable regularity to the same organs and parts? These are questions which for the present must remain unanswered. We may surmise that the activity of the germinal elements giving rise to the growths has been deferred by some error in development, and that

they have continued to grow in an abortive and spurious fashion long after their appointed term of expansion and metamorphosis; and we may imagine that development has been disturbed by some unknown intrauterine, infective disorder, having, like scarlet fever and many other diseases and conditions which could be named, a predilection for unrelated organs and parts.

But apart from these speculations, I submit that the data I have set down favour my primary assumption that the complex of changes characterising this disease is the outcome of some evolutionary aberration or disturbance arising during the last few months of fœtal life, affecting the endothelium of blood-vessels or lymphatics, and resulting in a form of structural hyperplasia and heterotopism.

I have added the word heterotopism to this definition to cover the occurrence of giant nerve cells in the growths affecting the cerebral cortex, and my concluding remarks will be devoted to a consideration of these elements. To say the least, their presence is puzzling, and unfortunately our knowledge of the development of the nerve cell is not advanced sufficiently to admit of a definite explanation regarding their origin. I have noticed, however, in my studies of the neuroglia cell in the growing brain, that at a certain stage of development—prior to the formation of the processes—it is difficult to distinguish between the young neuroglia cell and the young nerve cell; and, although there is no developmental evidence to show that under normal conditions nerve cells, like neuroglia cells, are derived from elements pertaining to the vascular system, still the similarity in structure during development is suggestive, and I cannot help thinking that an embryonic disturbance might lead to an occasional exchange of form, to the aberration in development and the heterotopism of which this disease provides examples. Finally, although these nerve cells are most interesting constituents of the cortical masses, there is not the slightest evidence that they are active factors in the production of the gliosis; on the contrary, their presence favours the original assumption that tuberose sclerosis is the ultimate manifestation of some evolutionary aberration or disturbance.

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Chapter 4.—Hypertrophy of the Cerebrum.

Synonyms.—Hypertrophic idiocy. Megalocephaly, macrocephaly.

Of these names hypertrophy of the cerebrum is in most common use, and, as I shall show presently, it fits histological findings: to the physiologist the name is not so apt, for whereas betterment of functional activity usually accompanies enlargement of an organ, the contrary is here the case.

It is wrong to describe tuberose sclerosis under the heading Hypertrophy of the Brain (*vide* "Quain's Dictionary of Medicine," last edition). By hypertrophy of the brain the majority of writers mean a specific disease in which simple, uniform enlargement of the organ, without definite lesion or cause, a state of cerebral gigantism, is the principal anatomical manifestation.

The correctness of including this condition in the category of sclerosis may be called in question. I do so, however, because certainly in the cases forming the basis of these remarks, induration was a pronounced feature, and I believe it has been so in all previously recorded cases. At the same time I recognise that the condition presents several important departures from the usual associations. In most forms of sclerosis shrinkage is an accompaniment, and for this shrinkage a proliferation of neuroglia or connective tissue is responsible; here, instead of shrinkage we meet expansion, and although, as I shall show, there is an undoubted proliferation of neuroglia, the disproportion between this and the induration is great. Further, the induration and the enlargement are general instead of local. And, touching causal factors, in the commoner forms of sclerosis an irritant, local or general, and a coincident destruction of nervous tissues have invariably been present, but in this disease we have no proof of the existence or action of an irritant and all the evidence is against any destruction of nerve tissue. It is evident, therefore, that we are face to face with an induration unique in kind, and obscure in origin.

Clinical Notes.

Case 1.—The first patient was a male, aged 29, who had been an inmate of Rainhill Asylum for fifteen years.

He was transferred from another asylum, and was without friends; hence no note concerning his family history or his childhood is recorded.

Being short in stature and having an immense head, a small trunk and delicate limbs poorly clad with muscles, he always presented a peculiar figure. All his movements were executed slowly, and he was readily fatigued, but there was no definite motor paralysis. So far as could be judged, cutaneous and special sensation were unimpaired. The commonly tested superficial and

deep reflexes were normal. No disease was detected in the organs of the trunk. He did not suffer from epilepsy, and there was no evidence of inherited syphilis.

Mentally he was an imbecile with a low degree of intellect; his vocabulary was so limited and his concepts so simple that he was quite unable to converse; he did not know his name or his age, and was rarely heard to say more than "give me a mug of tea." He smiled when taken notice of and evidently enjoyed some sense of conceit. A creature of spiteful impulses, he derived pleasure from attempting to injure aged and apparently feeble fellow-inmates, but, unable to discriminate between those who could retaliate and those who could not, and being weak himself, he received as much as he gave. He was unclean in his habits and addicted to self-abuse.

Necropsy.

As megalocephaly and hydrocephaly are sometimes confused during life, and I chanced to have at hand a hydrocephalic skull from a man of about the same age, I first made a series of comparative measurements. The figures are of sufficient interest to set down.

	Megalocephaly.	Hydrocephaly.	Difference.
Circumference	59·5 cm.	64·3 cm.	− 48 mm.
Glabello-occipital length ..	19·6 ,,	20·8 ,,	− 12 ,,
Basi-bregmatic height	14·1 ,,	15·5 ,,	− 14 ,,
Vertical index	71·90 cm.	74·50 cm.	− 2·60 mm.
Cephalic index	77·1 cm.	82·6 cm.	− 5·5 mm.
Minimum frontal diameter ..	11·2 ,,	11·6 ,,	− 4 mm.
Stephanic diameter	14 ,,	14·5 ,,	− 5 ,,
Asterionic diameter	12·5 ,,	11 ,,	+ 15 ,,
Maximum transverse diameter ..	15·2 ,,	17·2 ,,	− 20 ,,
Frontal longitudinal arc	14·6 ,,	19 ,,	− 44 ,,
Parietal arc	16·4 ,,	20·5 ,,	− 41 ,,
Occipital arc	12·4 ,,	6·7 ,,	+ 57 ,,
Total arc	43·4 ,,	46·2 ,,	− 2·4 mm.
Vertical transverse arc, right ..	19·4 ,,	20 ,,	− 6 mm.
Vertical transverse arc, left ..	18·7 ,,	21 ,,	− 13 ,,
Total transverse arc	38·1 ,,	41 ,,	− 20 ,,
Basi—nasal length	10·1 ,,	10 ,,	+ 1 ,,
,, alveolar length	9·4 ,,	9·4 ,,	0
Gnathic index	93·06 cm.	94 ,,	− 1·04 mm.
Asymmetry, frontal ..	R. + 4 mm.	0	
,, stephanic	R. + 10 mm.	0	
,, parietal	R. + 7 mm.	L. + 8 mm.	
,, asterionic	0	0	
Thickness of skull, frontal ..	10 mm.	3 mm.	+ 7 mm.
,, ,, occipital ..	12 ,,	5 ,,	+ 7 ,,

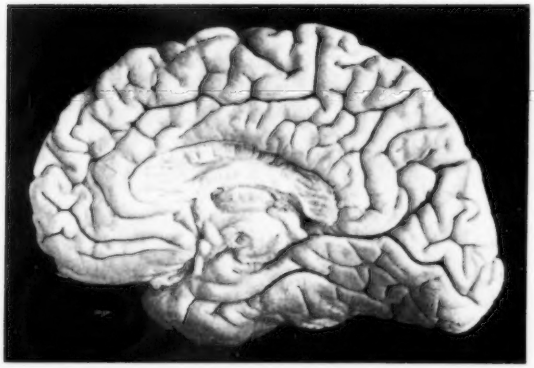

FIG. 5.

Hypertrophy of the Brain.

The inner surface of the right hemisphere from Case 1. In addition to the great size, the wealth of secondary sulci and the unusual distribution of parts in the region of the parieto occipital fossa are noticeable.

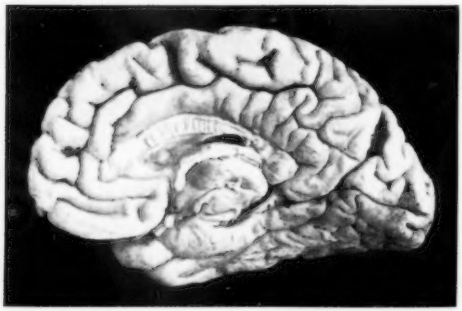

FIG. 6.

The inner surface of the right hemisphere of the brain (weight 1,350 gms.) from a normal female, for comparison with fig. 5.

These measurements do not diverge from what might have been expected, and they definitely prove that the brain enlargement in the disease we are considering is not associated with faulty growth of the cranial bones, as in hydrocephaly. The principal discrepancy affects the longitudinal arc; thus, although the frontal and parietal arcs were much greater in the hydrocephalic specimen, the collapse of the occipital bone, in the same skull, so reduced the occipital arc that the total measurements came to be approximately equal.

Passing to the cranial contents, the dura mater was normal, and there was no excess of cerebro-spinal fluid. The soft meninges were slightly increased in thickness and easy to strip, but free from opacity. The basilar artery appeared small, but the remaining trunks, and likewise the main veins, were normal in size and distribution, and I may mention here that microscopic examination disclosed no changes in them.

The brain was universally enlarged and scaled as follows:—

Encephalon	1,775	grms.
Right cerebral hemisphere (unstripped) ...	816	,,
,, ,, ,, (stripped) ...	775	,,
Left ,, ,, (unstripped) ...	768	,,
Cerebellum, pons and medulla	180	,,

The inequality in weight between the two cerebral hemispheres was not associated with any obvious asymmetry, the various lobes were well represented, in fact, the appearances of a large and uncommonly well-developed brain were offered. The surface colour was healthy, but handling proclaimed an abnormal and pronounced increase in consistence.

The form of the individual gyri was normal, and there was a complete absence of local atrophy on the one hand, and local hypertrophy on the other. On attempting to define the various named gyri and sulci, an arrangement of extraordinary complexity was found; indeed, in the whole of my experience, embracing a study of the morphology of several hundreds of brains intimately, and of several thousands casually, I have never seen one which presented such

a wealth of secondary sulci, nor one in which guesswork had to be relied on so much in defining even the constant and better known sulci. But, since a full gyrological account will be of more interest to the anatomist than the pathologist, and will overburden the present article, I reserve details for a future anatomical paper. Here, in connection with the photographs reproduced, I will merely indicate that the fissure of Rolando has a remarkable course, and that the usual guide to its identification, the cingular incisure, is misplaced; that the arrangement of parts in the quadrate and cuneate lobules is much disturbed by an abnormal disposition of elements constituting the parieto-occipital fissure or fossa; and that many fissures usually represented by simple lines are extensively ramified.

In my first notes of this case I find the statement, "wherever a sulcal annectant gyrus can come to the surface it has done so, hence the complexity of gyral arrangement." This, however, is not correct, because although, for example, it is true that the great arcus intercuneatus and much of the superior Rolandic annectant are exposed, the cuneo-lingual annectants in the posterior calcarine fissure and many others remain submerged. Therefore that assumption has been abandoned, and now, after more careful inspection, I favour the belief that the remarkable sulcal complexity has developed on common mechanical lines; I would insist, however, on one fundamental difference between this and the normal brain, namely, that while the richly convoluted brain of the sane individual results from the restricted expansion of healthy substance containing a normal admixture of constituents, we deal here with the expansion of matter having qualitative defects, defects to be described presently under the heading "Microscopic Examination."

The cortex generally was increased in depth, but it is interesting that several of the usual naked eye, topical variations in depth and appearance were noticed; for instance, the precentral cortex was appreciably deeper than the postcentral; of the frontal cortex the prefrontal was shallower than the rest, and in the visual area the line of Gennari was plainly visible.

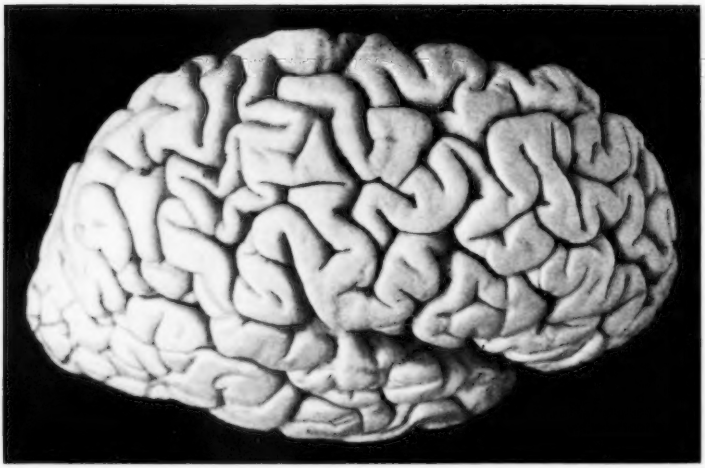

FIG. 7.

Hypertrophy of the Brain.

The outer surface of the right hemisphere, from Case 1.

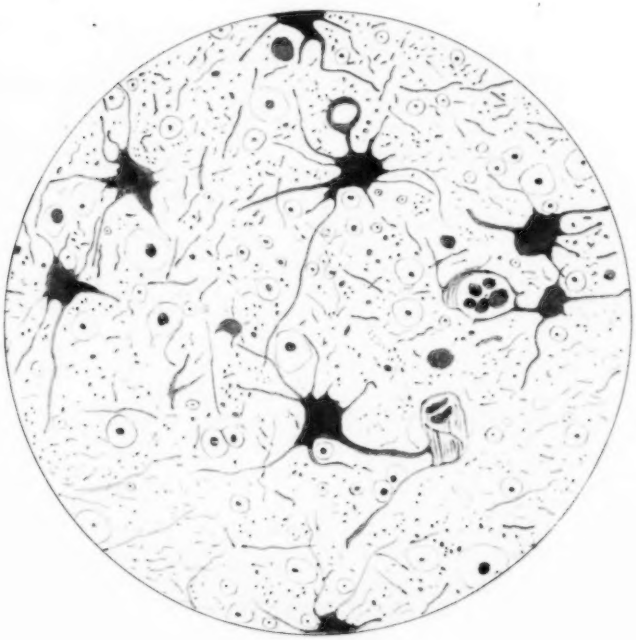

FIG. 8.

A reproduction of some of the large neuroglia cells present in the white substance of both cases of cerebral hypertrophy.

The white substance shared the general increase in bulk and looked healthy.

The lateral ventricles were not at all dilated; on the contrary, they were small in proportion to the size of the hemispheres; the ependyma was smooth. No abnormality of the basal nuclei could be seen. The corpus callosum was short, but stout. The anterior commissure was normal, the grey commissure smaller than usual. The septum lucidum, velum interpositum, choroid plexuses, and ventricular veins looked healthy.

The cerebellum, pons, medulla and spinal cord, were small in proportion to the cerebrum, but otherwise normal.

Examination of the trunk disclosed only the following points worth noting: a congenital malformation of the costal cartilage on the right side, the third and fourth being fused; universal plural adhesions, without thickening; œdema, congestion and some small gangrenous cavities in the lungs; old-standing mitral stenosis with much fibrous thickening of the cusps but little hypertrophy or dilation of the left ventricle or auricle; a small liver (945 grammes), congested and slightly cirrhosed, and congested spleen and kidneys.

Clinical Notes.

Case 2.—H. J. C., a male, aged 16, came from a private asylum, and again our record contains no reference to family or personal history.

Physically, no disability was apparent, and he was active in his movements.

A large but well-formed head and a bright expression suggested intelligence; on attempting to open a conversation, however, it was immediately discovered that he could neither speak nor understand the use of language; also, his general behaviour proclaimed a state of idiocy. He was mischievous; among other misdeeds he sometimes caused trouble by turning on gas and water taps, a product of imitation. When his wishes were not gratified, he displayed a vicious temper, and he was depraved in his habits.

It is remarkable that during the whole of his stay at Rainhill (five years) he did not have one epileptic fit, and yet status epilepticus—a series of forty-one seizures—was the cause of

Microscopic Examination.

The following account applies to both cases:—

(*a*) *Nerve Cells.*

Studying first the general lamination in sections taken from different parts and stained by the method of Nissl, it was astonishing not to find any positive abnormality. Whether taken from the frontal, parietal, temporal or occipital lobe, the sections showed an orderly columnar arrangement of cells, and both that disposition in layers and that representation of elements in the different layers known to characterise defined cerebral areas in the normal subject.

Going more into details I observed that the sectional outline of the cells, whether displayed by the method of Nissl, Golgi or Bielschowsky, was free from peculiarity, that the dendrons were normal in number and length, that in those cells which usually harbour chromophilic elements (Nissl bodies) such were visible, that when sections were silvered by the method of Bielschowsky neurofibrils appeared where they were expected, that there was no excess of pigment, and that none of those processless, pear-shaped, underdeveloped elements which we have seen in cases of idiocy were present.

Case of Macrocephalus.

	MM.		MM.
Layer 1	·278		·278
,, 2	·663		663
,, 3	·212		
,, 4	·236		·743
,, 5	·295		
Total	1·684 mm.		

An Average Normal Case in Paraffin.

	MM.		MM.
Layer 1	·27713		·27713
,, 2	·83616		·83616
,, 3	·24117		
,, 4	·23592		·77875
,, 5	·30166		
Total	1·89204 mm.		

death. The convulsions took the following form: during the first ten seconds, drawing up of the legs, clenching of the fists, half flexion of the arms and twitching of the facial muscles, all bilateral, occurred in succession; then followed snapping movements and biting of the tongue. The concluding clonic stage was prolonged and the apnœic exhaustion severe, so much so, that at the end of the sixth fit the lungs were already œdematous. The usual remedies were administered without benefit.

Necropsy.

The state of nutrition and the muscular and osseous development were normal.

The head measured 22 inches in circumference, 8 inches in the greatest sagittal diameter and $6\frac{1}{2}$ inches in the greatest bitemporal diameter. The forehead was high and the parietal bones expansive, suggestive of hydrocephalus. Placed anterior and internal to the parietal eminences were two additional symmetrical elevations as large as the parietal eminences. The interfrontal suture persisted. The calvarium was of normal thickness and the dura mater healthy. The pia arachnoid was opaque generally and thick, but not adherent. There was obvious congestion, but the vessels were normally distributed and had healthy walls.

For a boy of 16 years the brain was of great size. The encephalon weighed 1,515 grammes; the right hemisphere, unstripped, 672 grammes; stripped, 639 grammes; the left hemisphere, unstripped, 662 grammes; the cerebullum, pons and medulla, 145 grammes. The cerebral hemispheres were equal, and the representation of the lobes symmetrical and normal. The convolutions were perfectly formed, but the sulcal plan, without being abnormal, was complicated by many secondary ramifications, and various annectant gyri usually submerged appeared on the surface. The cortex and the white substance appeared to be healthy, but were distinctly increased in firmness. The ventricles were of normal size and the ependyma smooth. No fault was discovered in the commissures, basal nuclei, or remaining cerebral structures, and the same applies to the cerebellum, pons, medulla and spinal cord, though they were perhaps small in proportion to the cerebrum.

No change worthy of mention was found in the trunk.

(*b*) *Nerve Fibres.*

In sections stained by the method of Wolters-Kulschitzky I again saw nothing to associate with the defective mental state; indeed, had I been uninformed on the history of the sections and had I judged by the normal standard, I would have said that both the general supply and the arrangement of nerve fibres were those of an uncommonly well-developed brain.

(*c*) *Neuroglia.*

With the neuroglia it was otherwise, and yet the proliferation did not equal what reporters of other cases led me to expect. Nor, although the increase in glial elements no doubt contributed to the firmness of the cerebral substance, would I describe the condition as a gliosis. The microscopic picture was as follows:—

In the first or plexiform layer, a part wherein we find a decided excess of glial cells in another disease characterised by neuroglial proliferation, general paralysis of the insane, there was, it is true, some increase in the number of these elements, but it was not pronounced, nor did one see those great succulent cells so common in the disease named.

As is usual in other diseases, even in general paralysis, glial cells were not found in any number in the remaining cortical layers. In the white substance, however, it was different; here I have little hesitation in saying there was a true proliferation; moreover, on comparing the cells in these sections with the cells in sections from cases of advanced general paralysis, I observed very slight differences, structural or numerical. It did not matter how the sections were stained, whether by the method of Weigert, Bevan Lewis, Golgi or Bielschowsky, the cells stood out plainly, and I immediately classified them as homologous with the larger neuroglia cells of Bevan Lewis. As may be judged from the accompanying drawing the cells were of great size; they had many long, occasionally branched processes, and a stout vascular process ending in a sucker-like expansion on the vessel wall, and though the course pursued by the contained delicate, fibrillary elements seemed as usual to negative this,

there could be no question that the processes were attached to and formed integral parts of the cell; the body protoplasm was granular and relatively copious, and enclosed a large, round or oval, deeply-stained nucleus. (Fig. 8.)

Such, then, was the prevalent type of neuroglia cell; in addition to these, cells of smaller size were noticed, but I am uncertain whether they were not large cells which had undergone retrograde changes; also, there was an abundance of what are called nuclei of the neuroglia.

(*d*) *Blood-Vessels.*

In certain parts, for instance, the occipital region, the blood-vessels stood out prominently because they were congested, but nowhere were vessels seen with thickened or diseased walls—another difference from the condition found in general paralysis.

Review of the Manifestations of Hypertrophy of the Cerebrum.

Although megalocephaly must be reckoned a rare disease, the number of cases recorded from time to time has now reached well over double figures. I do not pretend to have read all the reports, but I will insert a list here showing the weights of some of the brains described; it will serve a purpose in demonstrating that while the brains in my cases do not approach the record they are still of extraordinary weight.

Reporter.	Sex and Age of Patient.	Weight of Encephalon.
Walsem	Male, aged 21	2,850 grammes.
Simms	Male, aged (?)	2,400 ,,
Anton	Male, aged 20	2,055 ,,
Obersteiner	Male, aged 8	1,920 ,,
Brunet	Male, aged 18	1,780 ,,
Grant	Male, aged 43	1,869 ,,
Campbell	Male, aged 29	1,775 ,,
Bernardini	Female, aged (?)	1,755 ,,
Fletcher Beach	Male, aged 15	1,754 ,,
Brunet	Male, aged 17	1,632 ,,
Campbell	Male, aged 16	1,515 ,,
Fletcher Beach	Male, aged 16	1,500 ,,
	Average ..	1,892

Running over the clinical manifestations we find that males are more disposed to the disease than females, that most cases die before reaching the age of twenty-one years, that a condition of idiocy or imbecility is invariable, and that when the latter is the case, although something of what is said to them may be understood, the receptive process is greatly delayed, while if they have learned the use of language their vocabulary is restricted and their words uttered slowly, without emphasis and in a low tone. In about fifty per cent. of cases epilepsy is a complication, and that disease is a common cause of death; indeed, it may be correct to say that after passing a number of years free, or almost free, from epileptic attacks, life is terminated by a series of convulsions (*cf.* my second case). Although this observation has not always been made, the head seems to be enlarged at birth, and during childhood dulness, drowsiness and headache are suffered from. Further, such children exhibit that inability to keep the head erect which results from inefficiency of the cervical musculature; and in this connection let it be noted, that not only may the head be too heavy to balance, but the neck muscles may be abnormally weak, for in other directions there is proof of muscular inactivity; thus, many of these cases are reported to have been as slow in learning to walk as they have been imperfect in muscular development and incapable of enduring fatigue.

Turning now to the pathology of the condition, it seems that not unfrequently these cases are tainted with an hereditary neurosis, and have brothers or sisters afflicted with idiocy or some other form of mental weakness. There is also abundant proof that the morbid process is active during intrauterine life; the large size of the head at birth, the presence of accessory parietal eminences and the persistence of the interfrontal suture which have been noticed, all signify abnormal cerebral growth at an early stage of development. Yet in searching for the cause further than this we cannot go. It is possible that the disease may rest on syphilis in the parents, but there is no certain evidence to that effect; indeed, it seems to me that not until a great many more observations are made and attention specially directed to

obtaining correct family histories, shall we light on the right cause of this disease.

Next, regarding histogenesis, in few cases has a microscopic examination been carried out, and in fewer cases still has the brain passed through the hands of a competent microscopist, hence the histology of the condition is imperfectly reported. In particular, I notice a tendency to write loosely of the presence of inflammatory sequelæ in the brain and meninges; thus one observer makes capital of a superficial encephalitis (whatever that may mean) of the anterior third of the brain; another, recording a case in which death occurred in status epilepticus, apparently is unaware that capillary congestion and "myelocytosis" are simply characteristic of the disease which proved fatal; again, some thickening of the cranial bones and firm union of the sutures have been wrongly given as evidence of chronic inflammation of the brain. But, in my opinion, the case for the inflammatory process has been greatly overstated. To begin with, it is a fundamental truth that we do not get inflammation without vascular affection, and yet to the best of my judgment the blood-vessels in the brains I have examined have been remarkably free from disease; as blood-vessels are particularly numerous in the pia mater, therefore chronic inflammation always manifests itself in the soft meninges, but the thickening, opacity and adhesion of these membranes, which we regard as post-inflammatory signs, have not been present in my cases. Again, inflammation necessarily brings in its train malnutrition, destruction and decay, and yet here we find the principal and the most unstable elements actually represented in increased numbers. Lastly, while neuroglial proliferation is a product of both inflammation and decay, and it cannot be denied that this tissue is unduly abundant in megalocephaly, still, as I have pointed out, there is a great disproportion between the degree of the proliferation and the size and induration of the brain; moreover, neuroglia is a supporting element, and it is significant that it is excessive in the white substance only.

To me it seems that much more importance attaches to

the proof we have that the enlargement of the brain is uniform and unattended by morphological imperfection. The architectural plan of the gyri and sulci may be unusual, but it is not bizarre; it is what we look for in the case of a person of high intellectual attainments, in accordance with the view that intellectual superiority runs hand in hand with advantage in cortical expansion. Inspection of known functional areas reveals nothing unexpected; for instance, on making a series of sections through the occipital lobe I observed that the area striata—visuo-sensory cortex—has a normal distribution; looking for giant "motor" cells, I find them where previous experience tells me they normally lie, and there only; indeed, the microscopic architecture shows no inconsistency in any part of the brain; in short, we have to deal with what seems to be a genuine cerebral hypertrophy.

In face of all these facts, the thought is forced upon us that this remarkable development of nerve cells, of nerve-fibres, and of cerebral nervous tissue in general, must be referred back to embryonic life, and tentatively I would suggest the influence of a developmental error. I would submit that there has been a deposit in excess of those embryonic elements which normally go to form the great system of cerebral neurones, a deposit quite out of proportion to standard requirements. Each primary specific centre (those for sight, smell, taste, touch and movement), each higher functional area, in fact the whole cerebral cortex, has been endowed with a wealth of fundamental elements far in excess of what is usual, and each element following a natural process has developed morphologically; but while development seems to have been good in so far as the central portion of the neurone is concerned, the same does not apply to the peripheral portion. To instance my meaning, let us take the motor area: for the perfect conveyance of impulses arising in the superabundant cortical motor elements, there should be a corresponding addition to the number of motor fibres in the motor tract; to the naked eye, however, the size of this tract in the medulla and in the spinal cord appears normal, and if, as is possible, there is an increase in

number of the individual fibres without an increase in volume of the tract, a point which I have not attempted to prove, plainly there must be an insufficiency of investing myelin on each fibre, hence insulation must be imperfect. Of necessity, the same defect must obtain in the case of fibres for the conveyance of special sensory impressions; while among the multiplied neurones pertaining to higher functional areas, that coupling together, that association essential to the smooth working of the cerebral machine, as a whole has remained imperfect. The apparatus has been unwieldy, too complex to assume normal functional activity and impossible to educate. Although, to continue my instance, the cortex is endowed with good motor cells, their perfect excitation has been impossible, and the resulting movements sluggish; similarly, the process of education leading to the execution of skilled movements, an example of the use of higher function, has been out of the question, while in higher spheres still, complications and counteractions, clogging mental processes, have produced the clinical picture of idiocy or imbecility.

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Chapter 5.—Cerebral Hemiagenesis or Hemisclerosis.

A diminution in size affecting one hemisphere alone, equally distributed, associated with sclerosis but unaccompanied by disarrangement of the gyral and sulcal architecture, outlines the anatomical picture in the condition now to be considered.

It is not uncommon to meet with brains on the *post-mortem* table in which there is a disparity of more than 100 grammes between the weight of the two hemispheres, and in which the asymmetry is sufficiently decided to be noticeable with the eye; but in the disease before us the disparity in weight and the asymmetry are profound.

The condition is rare; I have seen it once only, and the records contain accounts of few cases which I would place in the same category. The Index Medicus mentions several papers entitled "Cerebral Hemiatrophy," but on reading these I have discovered that the "hemiatrophy" was a reduction in size due to some local defect, a restricted area of microgyria, sclerosis and contraction round an area of destruction consequent on arterial embolism or occlusion occurring in early life, and so on—not hemiatrophy strictly speaking, and a state quite distinct from that with which we are concerned. Finding that the name "hemiatrophy" had been loosely attached to various diseases, it became necessary to employ a term which would distinguish the present condition, hence the name "hemisclerosis"; this, though physically proper, may not meet the approval of the pathologist, who, as I shall indicate in commenting on the condition, may prefer the term "hemiagenesis."

The case which I shall relate has already formed the subject of a note by Dr. J. Wiglesworth in the *Liverpool Medical Chronicle;* I have restudied the brain from the histological aspect.

Clinical Notes.

The patient was a female, aged 16 years, an idiot and a sufferer from epilepsy.

The clinical report gives no information touching the family history and is very imperfect It is stated, however, that the

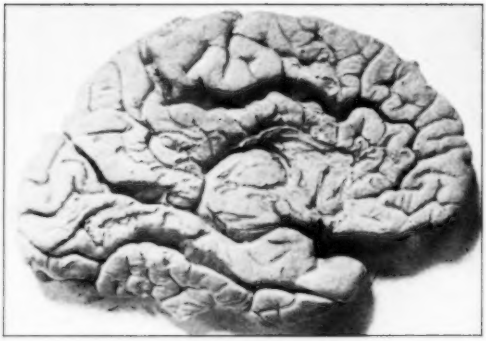

FIG. 9.

Cerebral Hemisclerosis.

Photograph of the inner surface of the left hemisphere.

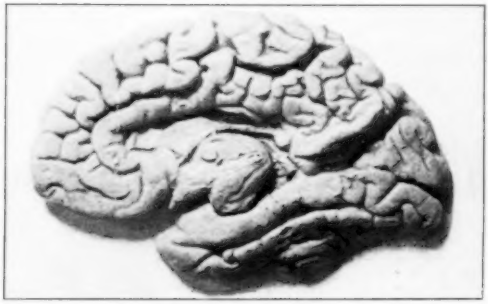

FIG. 10.

Photograph of the inner surface of the right hemisphere illustrating the asymmetry in the author's case. Although the sclerosed right hemisphe ɔ is so much the smaller it has preserved its form.

extremities of the left side were small and "shrivelled," and that talipes varus on the left side, and genu valgum on the right, made walking impossible, although the patient could stand. What power of movement she had in the wasted limbs is not mentioned, nor do the cutaneous and special senses seem to have been tested.

Necropsy.

The brain scaled as follows: Encephalon, 800 grammes; right cerebral hemisphere, unstripped, 218 grammes; stripped, 198 grammes; left cerebral hemisphere, unstripped, 417 grammes; stripped, 405 grammes; cerebellum, pons and medulla, 112 grammes.

The disparity in size and in weight between the cerebral hemispheres were features of dominant interest in the case. They were accompanied by many secondary changes in the cranium, but I need mention only that the right half of the head was obviously smaller than the left, and that this applied to the bones of the vault as well as to those forming the basal fossæ. In thickness and in density and as regards sutures, the bones were normal. So was the dura mater, save that a pale pink film,[1] composed of migratory and red blood cells, lined the vault on the right side. There were no abnormal adhesions between brain and dura. The cerebro-spinal fluid was not markedly excessive. The pia-arachnoid membrane covering the right hemisphere was thick and opaque, and stripped in one sheet; that covering the left hemisphere was normal. The main arteries of the right side were smaller than those of the left. Anæmia was general.

Comparing the cerebral hemispheres (*vide* figs. 9 and 10), it was remarked that although the right was so greatly deficient in size it was not strikingly altered in form; every convolution was attenuated, every sulcus gaped and was shallow, all the basal nuclei were small, the white substance was wasted and the lateral ventricle dilated, but the general architecture was undisturbed, and it could not be said that any lobe or part in particular had suffered more than the rest. There was a striking difference in consistence, the

[1] This had no bearing on the principal change; such films are common in phthisis, the disease which caused death

lesser hemisphere throughout was greatly increased in firmness, cutting almost like costal cartilage; the same hemisphere was pale and pearly in appearance, and its cortex shallow and indistinctly striated. In all these respects the opposite hemisphere was approximately normal.

Consequent on this cerebral asymmetry and the deficiency of cortical nerve cells and central nerve fibres, there were changes in related parts. The contralateral cerebellar hemisphere was distinctly reduced in size; the corresponding motor tract throughout the mesencephalon and spinal cord was wasted, and the lemniscus presented the attenuation of retrograde atrophy.[1]

The changes in the trunk included severe chronic tuberculosis of the lungs, secondary tuberculous ulceration of the intestine, and lardaceous degeneration of the liver, spleen and kidneys.

Microscopic Examination of Cerebral Cortex. (Fig. 11).

(a) Nerve Cells.

A careful examination of many pieces taken from corresponding parts of both hemispheres revealed uniform changes throughout the affected half. On the whole the cells preserved their columnar arrangement and the individual members their erect attitude, but the cortex was reduced in depth by quite two-fifths, and the lamination altered in the following manner.

The plexiform layer (1) was very thin.

The small pyramidal cells (2) were deficient in number.

The numerical deficiency fell even more heavily on the medium-sized and large external pyramidal cells (3 and 4), and the shallowness of the combined layers struck the eye immediately; moreover, few elements persisted here which might be described as normal; the majority were small and round, or oval, instead of pyramidal, their processes were stunted, they lacked spongioplasm and were achromophilous. Such cells recalled alike the neuroblasts seen in the deve-

[1] I investigated the changes in these parts very carefully, but do not describe them at length because they were an exact replica of what we have often seen in other cases of unilateral cerebral defect.

loping brain, the stunted elements in cases of idiocy, and the atrophied cells in specific centres altered by interruption of incoming stimuli (cases of old-standing deafness or blindness, of tabes dorsalis, &c.).

A few small cells remained to mark the position of the stellate layer (5).

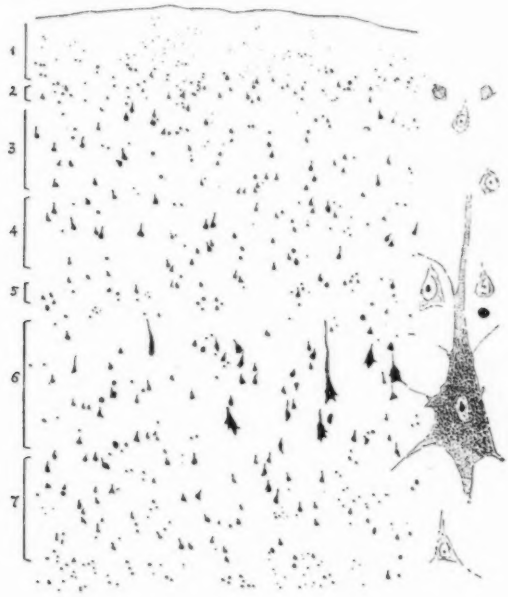

FIG. 11.

Camera lucida drawing of the cell lamination in the cortical motor centre for the leg in the diseased hemisphere. The cortex is shallow, the reduction in depth mainly affecting the suprastellate layers.

It is a remarkable and important feature that in cortex where the cells of the next layer—the internal layer of large pyramidal cells—are specialised, such cells persisted and showed but minor alterations. For instance, in the motor cortex, which I illustrate, the preservation of the giant cells was astonishing; their figure was attenuated, but their number good; the method of Nissl showed chromophilic elements diminished in size, but not true chromotolysis, and

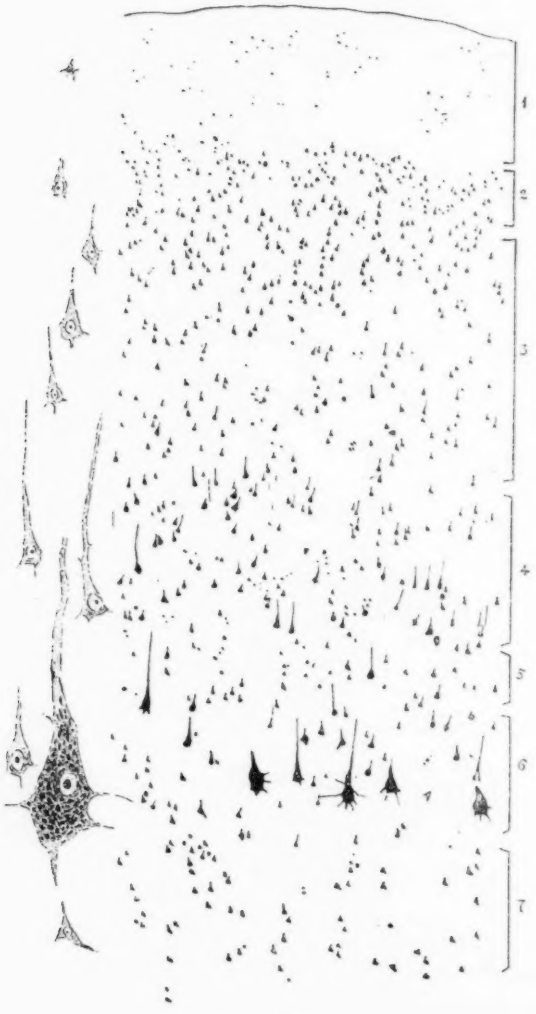

FIG. 12.

Camera lucida drawing of the cell lamination in the cortical motor centre for the leg in the normal hemisphere of the author's case of Hemisclerosis for comparison with Fig. 11.

the method of Bielschowsky revealed both a wealth of neurofibrils[1] and normal processes. Similarly in the visuo-sensory, in the postcentral and in the olfactory areas, areas wherein homonymous specialised cells are found, these among the cells of all other luminæ, save the fusiform layer, showed the best state of preservation.

The last layer, that of the fusiform cells, could be included with the layer just considered as preserving its constituents fairly intact.

Most of the points regarding cell lamination that I have mentioned are illustrated in the accompanying figures. The significance of the changes will be discussed in a later section.

(*b*) *The Blood-vessels.*

I searched many blood-vessels for signs of past inflammation, but the quest was negative. The vessels were not more numerous than usual, nor did thickening or over-cellularity of their walls cause them to stand prominent; also, signs of syphilitic endarteritis and of hyaline and other forms of degeneration were not in evidence.

(*c*) *The Nerve Fibres.*

Examining the nerve fibres as carefully as I examined the nerve cells, I again found changes in the lesser hemisphere as pronounced as they were universal.

The zonal layer in all regions, even in the motor area, where it is so prominent in the normal brain, was reduced to the palest of bands, made up solely of a few varicose fibrils. The supraradiary layer was correspondingly poor. A line of Baillarger was scarcely visible.[2] The radiations of Meynert, instead of being stout and composed of many large medullated fibres (I refer to the motor cortex) were

[1] The persistence of the neurofibrils is not easy to explain. In other conditions I have displayed them in cells quite denuded of Nissl granules. Evidently more information is needed regarding their nature and significance.

[2] In my "Histological Studies on the Localisation of Cerebral Function," I pointed out that the line of Baillarger lay on a level with the external large pyramidal cells, and that its representation varied proportionately to the representation of these cells. The condition of the line in this brain accords with that observation.

attenuated, made up of coarse varicose fibres, and seldom strengthened by a normal evenly-medullated fibre.[1]

The interradiary spaces were almost empty, even in parts like the motor area, where in the normal state they are packed with fibres.

In short, a general loss of fibres was apparent, and I think it correct to summarise with the statement that the deficiency fell most gravely on the various systems of association fibres.

(*d*) *The Neuroglia.*

Large active neuroglia cells like those seen in the white substance of the normal brain were scarce; in all parts, however, there were numbers of the smaller variety of cell, as well as an abundance of so-called nuclei of the neuroglia, also the glial feltwork was uncommonly dense. The condition suggested a past glial proliferation to compensate the cell and fibre deficiency.

The origin of this condition is not easy to discover, and several speculations have been urged concerning its pathology; these we will briefly consider.

The weak suggestion has been advanced by one writer that it may be the outcome of unilateral narrowing of the carotid canal. No doubt narrowing of this canal will reduce the flow of blood along the middle and anterior cerebral arteries, and if it occur early in life may well interfere with the development of the parts of the brain nourished by these vessels; but surely coincident obstruction of the homolateral vertebral artery by narrowing of the foramen in the atlas, and over and above these constrictions, anastomotic imperfections, such as inelasticity of the Willisian arteries of

[1] It may seem incongruous that in the motor area, where the giant cells were preserved, the radiations of Meynert were attenuated. It will be remembered, however, that while these cells retained their shape they were reduced in size and showed internal alterations. And I have little doubt that if it had been possible to trace the axon of one of these cells, it would have been found attenuated and wanting in myelin. This supposition is consonant with an observation I made to the effect that the wasted pyramidal tract leading from the affected hemisphere retained a blue tint, instead of being decolorised, in Weigert-Pal specimens, and that on microscopic inspection the contained fibres, though not wholly amyelinic, were mainly composed of axis cylinder.

communication, would be necessary to make the wasting of the hemisphere complete. There is no proof of any such obstructions, so that the suggestion need not be further pursued.

Of unilateral synostosis of the cranial bones preventing cerebral expansion there is likewise no evidence.

Injuries at birth are fruitful sources of brain lesions, and syphilis in parents or child are disease-producing factors always to be kept in view; here, however, we have no trace of the operation of either agent.

An attack of meningitis during infancy is more deserving of consideration, because we can readily believe that such an inflammation will not pass away without affecting the calibre, the elasticity, and the carrying capacity in general of the main arteries. This, notwithstanding there are several objections to meningitis as a cause of the condition of the case before us. In the first place, meningitis is not a disease which confines its attack to one hemisphere, and touching its effect on the main arteries, although in the majority of cases it attacks the base of the brain and involves the arterial trunks, it is as difficult to believe that it can confine its operations to the arteries proceeding to one hemisphere as it is to think of it spreading over one hemisphere and leaving the other intact. And yet other writers, particularly those of the German school, who lay stress on antecedent meningitis as a source of various changes which we see in the brains of idiots, might give causal importance to the thickening and opacity of the meninges noted in this case. To this I can only reply that the condition of the membranes did not suggest past acute inflammation; it reminded me of what I have observed repeatedly in the brains of the chronic insane, especially those afflicted with severe dementia, a condition of obscure origin, but certainly not the product of acute meningitis. The microscopic appearances, also, did not favour meningitis; in the cortex of this hemisphere we saw that, while cells and fibres were deficient, they were not arranged in a disorderly manner; the radiary fasciculi of fibres pointed straight towards the surface, and the cells stood erect and in column formation. This would not

have been the case had meningitis pre-existed; in that event it would have been in accordance with our experience to have found the uppermost laminæ swept bare of cells and fibres, contracted and converted into connective tissue; moreover, from unequally distributed obliteration of cortical arterioles, patches of cortical destruction surrounded by contraction changes would have been seen in the deeper parts.

Having disposed of these preliminary speculations, we can now pass to the consideration of a problem which, in my opinion, it is of fundamental importance to solve. Did the condition exemplify atrophy of a part previously well developed, or was it the outcome of arrested growth? In my opinion it was the latter, and the following observations strengthened my belief. In form and in size the hemisphere resembled that of a full-term fœtus, but it was from the microscopic rather than the naked-eye appearances that I derived chief support for my contention. When studying the cell lamination we were struck with the fact that cells beneath the stellate layer, namely, the polymorphic and the internal large pyramidal cells, were preserved, whereas the cells above the stellate layer, in particular the medium-sized and large pyramidal cells, were very weakly represented, and to deficiencies in these layers we thought that the shallowness of the cortex was mainly due. Let us compare this with the state in the fœtal brain. As Dr. Bolton has proved, if the cortex of a fœtus be measured beside that of an adult, exactly those layers in the former will be shallow which were found to be so in this case; the corollary follows that the suprastellate pyramidal cells are the last to develop. Turning to deeper cells, it is well known that comparatively early in intrauterine life the specialised large pyramidal cells peculiar to certain areas—the cells, be it noted, which persisted in this case—may be recognised, and that the fusiform cells, likewise persisting in this case, are not much later in making their appearance. The resemblance, so striking from this standpoint, does not end here. From the writings of Flechsig, Kaes, Vulpius and others, who have studied the myelinisation of the cortex

of the growing brain, we learn that the tangentially-directed fibres, the supposed association fibres, become invested with myelin considerably later than the vertically-placed projection fibres. A replica of this stage of development was seen in this brain; the radiary fasciculi, though deficient in myelin, were fairly prominent; the zonal layer, the line of Baillarger, and the association fibres, on the contrary, were barely recognisable, and this even in parts where normally they stand out with the greatest plainness. Furthermore, the amyelinic condition of the fibres composing the pyramidal tracts was a reproduction of the fœtal state.

While maintaining that all these microscopic revelations favour my thesis that the defect in this instance is ascribable to arrest of development, it does not escape my mind that some of these data may be seized upon by those who favour the view that the condition is the outcome of atrophy. In particular I recognise that an attempt may be made to explain the deficiency of stellate cells on the ground that, being highly organised elements and the last to develop, so they are the first to disappear in processes of degeneration. This is an axiom the truth of which cannot be gainsaid. Also, I will not deny that in cases of atrophy the change is dominant at the level in question; but in all my experience of cortical wasting, I have not yet met with a case in which other layers besides the suprastellate have not shared the change, in which, to be more precise, the specialised substellate pyramidal cells, the fusiform cells and other elements, have not exhibited pigmentation, swelling, disintegration, numerical deficiency, and many other signs of degeneration. In this manner, therefore, wasting differs from the condition in hand. Further, and this is an important point, the profound asymmetry of the cranium contraindicated atrophy of its contents as strongly as it suggested their restricted growth.

Accordingly, I submit that we have to deal here with a true case of arrest of development, that the original deposit of elements going to form the nerve cells and nerve fibres was not deficient, and that growth proceeded normally until just before, at, or soon after birth (the conformation of the hemi-

sphere is preserved), but then ceased; that the elements subserving primary essential functions, being developed already, persisted; that the elements subserving higher evolutionary functions, being only partially developed, and therefore unstable, to a large extent, but not wholly, suffered decay, and that coincident with this decay the neuroglia proliferated, hence the sclerosis.

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Chapter 6.—Lobar Agenesis with Sclerosis and Microgyria.

I will now pass on to another remarkable condition, which from the standpoint of pathogeny I would classify with cerebral hemiagenesis, because, in my opinion, it is likewise a manifestation of arrested development. Anatomically it differs from hemiagenesis in being bilaterally distributed; but it bears a resemblance to this condition inasmuch as the gyri of the affected lobes, though attenuated and sclerosed, are not puckered, and the plan of the sulci is not disarranged.

Lobar sclerosis and lobar microgyia may be suggested as better names for the condition. I must point out, however, that these names have been affixed indiscriminately to cases of lobar sclerosis resulting from intrauterine destructive lesions (really cases of porencephaly), to the contraction and induration occurring round an old and extensive patch of cerebral softening, to postmeningitic atrophy and sclerosis, always without regard to the exciting factor, where the sclerosis or microgyria is but a sequel of the primary disease. This is surely wrong, and, in my opinion, now

that our knowledge of the anatomy of the brain in idiocy is becoming more stable, it will be better either to abandon the titular use of these names, or to reserve them for conditions (they must be very rare) in which the sclerosis or the microgyria, being the primary and essential feature, is deserving of capital mention.

I am fortunate in having three specimens with which to illustrate my remarks. Of the subjects two were females, aged 17 and 32 years at death respectively, and one a male aged 35 years at death. All suffered from epilepsy, and though their mental state, as observed in Rainhill Asylum, suggested idiocy, a history of the display of a certain amount of intelligence during childhood proves that they were not cases of congenital amentia. Since the anatomical picture in all the specimens is alike, it will not be necessary to describe more than one in detail. I choose that from the female, aged 32 years, because it was the last observed.

Clinical Notes.

The patient was admitted to Rainhill Asylum at the age of 16. The mother informed us that there were four other children in the family, all healthy, and that this girl had attended school and been apparently normal until the age of 12, when she began to suffer from epilepsy. This was the signal for a mental deterioration so rapid that three years later she was completely demented and in need of asylum restraint.

On admission to Rainhill she would have been classed as a case of congenital amentia had no details concerning her earlier life been forthcoming. She seemed to understand nothing of what was said to her, she took no interest in her surroundings, and either would not or could not speak. No physical defect was discovered except some weakness of the left arm, and this proved to be transitory.

The further course of the case was devoid of interest. In summary form the notes state that she was a petulant, degraded, coprophagic ament, and a sufferer from frequent and severe epileptic fits.

Necropsy.

Though short in stature the limbs and trunk were duly proportioned, well clothed with muscles and free from

deformity. The fat covering was normal and the mammæ were fairly developed. There were no traces of congenital syphilis. The scalp was thickly covered with coarse, black, curly hair. In the shape of the head and face there was nothing peculiar, and in regard to cranial size the following measurements are illustrative:—

Circumference of head	55 cm.
Arc measurement from glabellum to occipital protuberance	33 ,,
Arc measurement from ear to ear	30 ,,
Greatest transverse diameter	14·3 cm.
Greatest antero-posterior diameter	18·5 ,,
Cephalic index	77 cm.

The calvarium was very thick, yielding average frontal and occipital measurements of 12 mm. and 11 mm. respectively; the increase in thickness mainly affected the inner table; the structure of the bone was fairly open, and the thickening seemed to be compensatory. The lines of the meningeal arteries, strange to remark, were not deep. A groove of normal depth and breadth accommodated the superior longitudinal sinus. The sutures were close, but not obliterated. Broad furrows, following the lines of the sutures, which we have learned to associate with syphilis, were not present.

The dura mater and its sinuses were normal. A slight excess of subdural fluid was noticed. The main arteries, carefully inspected, were only a little more delicate than usual. The pia covering those gyri to be noted presently as attenuated, was somewhat thickened and easily stripped, elsewhere it was normal.

The cerebrum exhibited remarkable bilateral alterations affecting the frontal and parietal lobes.

The Frontal Lobes.

The frontal lobes in each hemisphere and almost symmetrically were greatly diminished in size; viewed from above they stood apart from one another; from the side they looked pointed and the orbital face was tilted outwards. Excepting the precentral or ascending frontal gyrus, which was normal in each hemisphere, not one convolution on the

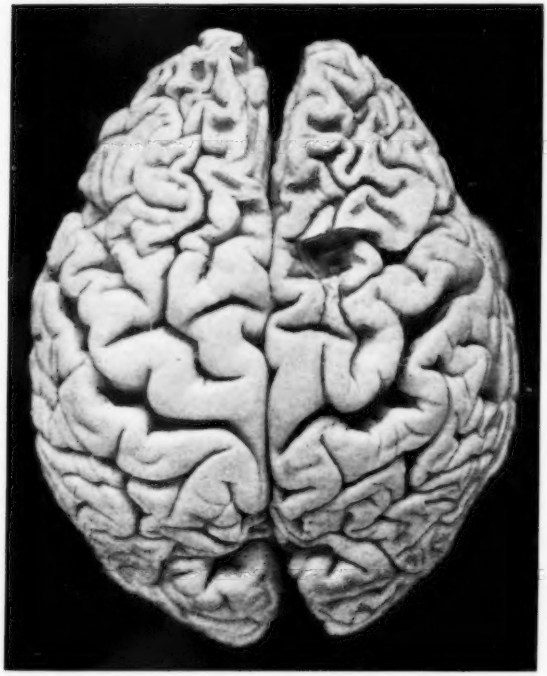
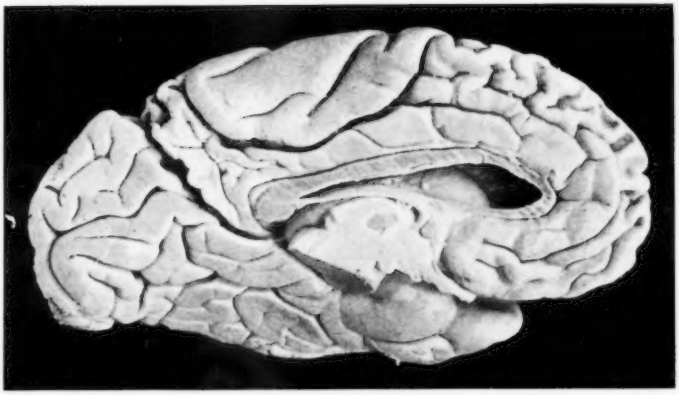
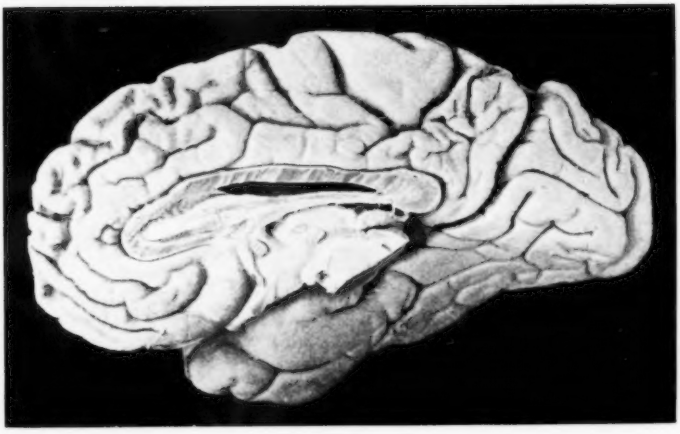


FIG. 13.

Lobar Agenesis with Sclerosis and Microgyria.

A view of the upper surface of the hemispheres in Case 1, showing the wasted frontal and parietal lobes.





FIGS. 14 AND 15.

Lobar Agenesis with Sclerosis and Microgyria.

The inner surface of the hemispheres in Case 1. Observe the bilateral and symmetrical attenuation of the gyrus marginalis and the precuneus; also, the large relative size of the oval lobule.

convex surface had escaped attenuation; the degree varied; those most changed were wormlike, pale brown and tough. those less affected, white and not so tough. On the mesial surface the marginal gyrus alone suffered, the oval lobule and the gyrus cinguli being normal. On the orbital surface all gyri, excepting those bounding the sulcus olfactorius, shared the change.

The Parietal Lobe.

Save the postcentral gyrus and its paracentral annexe which, like the precentral gyrus, were normal, the whole lobe was diminished in size and microgyrous. On the mesial surface the withering was very pronounced, but restricted in a most extraordinary manner to the precuneus and to that portion of the postcingular gyrus with which it stands connected. On the convex surface the wasting was less, and yet the superior parietal gyrus and the upper parts of the supramarginal, angular and posterior parietal gyri, were much below the normal size.

The Occipital Lobe.

The external occipital gyri were slightly attenuated, but those on the minor surface healthy.

The Temporal Lobe.

The temporal lobe stood out in that it was unaffected. The insular likewise remained untouched.

The Limbic Lobe.

The lobus pyriformis and all parts in the regio olfactiva were normal.

The corpus callosum, the fornix and the anterior and posterior commissures, were all slightly attenuated. The anterior horns of the lateral ventricles were dilated. The crura cerebri were small, but equal.

In the cerebellum some folia of the lobus clivi and others along the great horizontal fissure were wasted and unduly firm, apparently having undergone changes not unlike those in the cerebrum.

The heart was the only diseased organ in the trunk; it presented mitral stenosis (·45 inch), but evidently this was very old and had been naturally compensated, for the heart weighed only 243 grammes, and the size of the chambers relative to one another and the thickness of the walls was not greatly altered.

Microscopic Examination.

(*a*) *Nerve Cells.*

Portions of different gyri were examined, but to instance the changes I will take the condition of the cortex at the base of the superior frontal gyrus (regio precentralis intermedia of the author).

We have seen in our study of other brains that the cell laminæ most prone to decay are those which are the last to appear in embryonic growth, namely, the small, the middle sized, and the external large pyramidal cells (layers 2, 3 and 4). Exactly these laminæ were most deficient in this brain, and their weakness accounted for some thinning of the supraradiary plexus and the line of Baillarger to be noted presently. Of the internal large pyramidal cells many persisted, but they were all much reduced in size, and in addition so intensely chromophilous that even the nucleus was barely visible. The layer of fusiform cells, which is early to develop, which is constant throughout the animal series, and which is very resistive to decay, was the best preserved of all the layers. Lastly, the cell changes were evenly distributed, that is to say, the disorder and the patchy affection seen in inflammatory and vascular lesions were absent.

(*b*) *Nerve Fibres.*

The general fibre wealth of the cortex and of the medullary projection was greatly diminished, but of chief interest was the finding that the association system of fibres had suffered much more that the projection system. Thus, even in gyri which were most wasted, the radiations of Meynert, although attenuated to a considerable extent, were still prominent objects in the field, and they were

strengthened by a few large medullated fibres, doubtless the axons of the remaining large pyramidal cells, and some large varicose fibres. The interradiary spaces, on the other hand, were comparatively empty; in particular they were quite bereft of those long, oblique or horizontal, large medullated fibres, which we look upon as associational or internuncial in function, and which are usually present in abundance in this situation.

As a feature of minor interest, the absence of a zonal layer, a wasted supraradiary layer, and a scarcely recognisable line of Baillarger were noticed, and, lastly, I will again emphasise the points that the radiary fasciculi stood erect, and that the signs of architectural disturbance were wanting.

(*c*) *Neuroglia.*

Neuroglia fibrils and so-called nuclei of the neuroglia were abundant in the diseased parts, and explain their firmness; but there were no large active neuroglia cells.

(*d*) *The Blood-vessels.*

The blood-vessels as seen in these sections showed no change calling for special remark.

Commentary.

In our search for enlightenment concerning the origin of the changes illustrated by these three brains, the first, indeed, the fundamental, point for consideration concerns distribution. In each specimen, with remarkable symmetry, precision and uniformity, the process is distributed over and restricted to the frontal and parietal lobes; in the former all gyri suffer, excepting the gyrus precentralis and some on the orbital surface; in the latter the postcentral gyrus alone escaped, and the precuneus is singled out for specially severe affection. To explain this distribution the series of causal factors from which we may choose includes vascular obstruction of different kinds, trauma, specific forms of inflammation and anomalies of growth and development.

The first factor, vascular obstruction, deserves careful consideration, because to the morbid anatomist the naked-eye appearance of the altered gyri at once suggests nutri-

tional disturbance. Regarding this suggestion it is obvious that if there had been a reduced supply of nutriment, it must have been due to an affection of either arteries or veins, and if the former the cerebral changes should present an arterial distribution. But here at the very outset we meet an insuperable obstacle, the required agreement in not forthcoming. The atrophied gyri in the frontal lobe derive their blood supply partly from the anterior cerebral and partly from the middle cerebral artery, but not once in an examination of several hundred cases of softening from embolism and thrombosis of varying origin which have passed through my hands, have I seen a lesion having this distribution, even in one hemisphere, much less bilateral. Not only does it so happen that this part is one which is seldom the seat of a localised softening (a widespread softening from plugging of the anterior or the middle cerebral artery is of course not uncommon), but it is impossible to believe that the twigs to this field should be selected for occlusion and other branches of the same arteries left open.

Under the same premise the parietal defect is still more difficult to explain, because a part is wasted which draws its blood from all three cerebral arteries.

The microscopic appearances still further negative this suggestion. I have stated that there was no distortion of the general cortical architecture, that the cells preserved their columnar arrangement, and that the projection bundles of fibres stood erect, and, in my experience, gyri attenuated and sclerosed as a result of deficient blood supply, for instance, those on the borders of an old patch of softening, are never free from this distortion. For these reasons I regard arterial obstruction as an untenable hypothesis.

Turning to venous obstruction, there is one condition worth more than passing notice, thrombosis of the superior longitudinal sinus. In several cases of thrombosis of this sinus which have come under my observation, I have noticed that the congestion and the resulting multiple capillary hæmorrhage have favoured special situations, namely, the parietal and the frontal lobes on the convexity, and it has

been interesting to see, presumably on account of the cross anastomosis along the veins of Trolard, that the two central gyri, just as in the cases under notice, escaped. Bearing these observations in mind, I can imagine that if a thrombosis of the superior longitudinal sinus were recovered from —it is usually fatal—and the obstruction persisted, or only imperfect recanalisation of the thrombus took place, it would exert an atrophic influence on the parts in which we are interested. But, unfortunately, I have no evidence to put forward to prove the occurrence of this thrombosis, my suggestion is purely speculative. The condition of the superior longitudinal sinus is not always noted at an autopsy, and it was overlooked in one of my cases; in the other two, however, I satisfied myself that the channel was apparently normal at death, whatever it may have been previously.

Touching trauma as an agent, all our evidence is negative. I suppose we may take it for granted that the chief manifestation of an injury is a rupture or thrombosis of blood-vessels; here there are no hæmorrhagic residua, and reasons have been given which render antecedent rupture of arteries unlikely.

Meningitis, encephalitis, and other inflammatory conditions, as possible causes of altered nutrition and subsequent atrophy, are all similarly disqualified by the remarkable distribution of the change.

Having found none of these hypotheses sufficient to explain the condition, we will lastly discuss the possible influence of a developmental defect, and now several very interesting points will be presented for consideration. One feature of great importance meets the eye when we view these brains from the aspects of physiology and comparative anatomy; selecting first the negative side of the picture, the side showing the parts which are preserved as against those diseased, we observe that the intact areas are precisely those we have recognised as designed for the control of movement and for the reception of the different sense impressions, in other words, for the government of those simple functions common to and used as a means to survival by all animals; thus, the visual area in the occipital lobe, the lobus

pyriformis, representing the chief known centre for smell; the central gyri for the control of movement and for the registration of cutaneous sensations; the gyri of Heschl and the temporal gyri concerned with hearing, are all plump and healthy. Turning to the positive side, we notice that the parts destroyed are those which have been the last to appear in the progress of phylogenetic development, and which are elaborated for the government of those higher psychic functions and faculties possessed by man alone, and making him pre-eminent among terrestrial animals. In other words the specimens afford a pregnant illustration of a reduction towards the elementary state obtaining in the lower mammals.

This view of the brain is full of instruction. It seems to be a general physiological truth that structures and parts whose development, alike in the ontogenetic and in the phylogenetic sense, is deferred, are designed and specialised to subserve high evolutionary functions; likewise we may regard it as a natural law that the same structures and parts are penalised for their greatness by being the first to deteriorate, both in the normal process of dissolution and decay, and when the organism is subjected to an adverse and devitalising environment. In the case of the brain the frontal lobes, excluding the motor area, and the parietal lobes may be pointed to as being the last phylogenetic addition to the central nervous apparatus, and it is an established truth of ontogeny that they are the latest to acquire their fundamental nerve cell and nerve fibre constituents. On these grounds I maintain that the withering of these very parts in the specimens before us must be more than a coincidence. I submit that the wasting is not the product of any of the ordinary locally-acting morbid factors, but the manifestation of an unnaturally premature decay of parts constitutionally disposed to early dissolution, and at the same time specially susceptible to the effects of evil hereditary influence or any other adverse agent which may proclaim itself during the progress of either pre- or post-natal development. On this and no other ground that I can think of can we explain those features which puzzled us before, the bilateral, symmetrical and altogether remarkable distribution of the change,

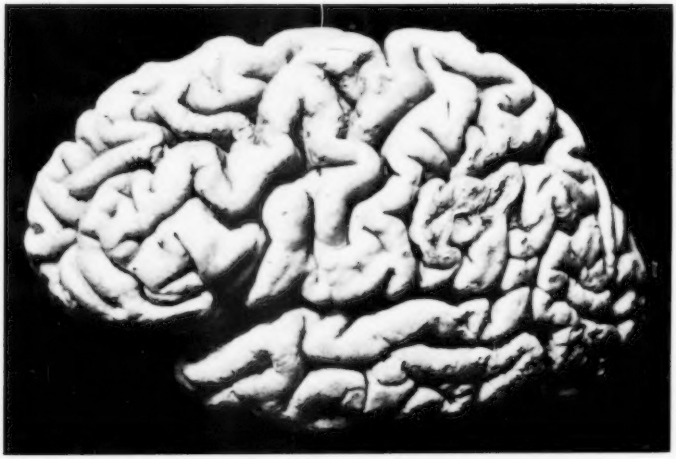


FIG. 16.

Cerebral Arterio-Sclerosis.

A photograph of a cerebral hemisphere, showing puckered gyri in the frontal and parietal lobes.

the perfectly preserved architectural plan of the affected gyri and the well-ordered arrangement of cortical elements as seen through the microscope.

Chapter 7.—Cerebral Arterio-Sclerosis.

The morbid process now to be considered is chiefly of interest to the anatomist and histologist. In all parts of the brain, but especially on the outer surface, convolutions, or portions thereof, are irregularly picked out for attenuation and sclerosis; at the same time the surface is puckered by many minute pits and linear or radiate cicatrices, and withal the form of the gyri is not wholly lost.

As gyri in a similar state may be observed around patches of softening from arterial embolism and thrombosis, it must be explicitly stated that the present cases were independent of any gross lesion.

The condition is not common; although my experience has been among the insane, in whom cerebral lesions of all kinds are more frequent than in the sane, in a sequence of more than two thousand autopsies I have obtained only four specimens.

I will now enumerate briefly the leading features in each case.

Case 1.—A male, aged 24 years, who suffered from dementia with epilepsy. Both hemispheres were affected, the right more than the left. Analysing the distribution of the shrunken gyri, it was noticed that most lay within the area of supply of the middle cerebral artery, exceptions being some in the retrocalcarine region, pertaining to the posterior cerebral artery. The changes had not altered the plan of the fissures, and yet they must have been of old standing, because the cerebral disparity was accompanied by corresponding cranial asymmetery. The distribution suggested that the condition might have resulted from partial arterial occlusion such as arises in syphilis, notwithstanding that we could produce no evidence of syphilitic infection. Death was ascribed to phthisis.

Case 2.—A female, aged 80 years, who suffered from dementia with epilepsy. The withered gyri were scattered over the posterior and upper parts of the frontal lobes, the parietal lobes and precunei, and along the external parieto-occipital boundary. The

arteries of the brain, indeed, of the whole body, were exceedingly atheromatous and calcareous, the basal nuclei showed *état criblé*, and there were a few small scars in the centrum ovale.

Case 3.—An obese woman, aged 64 years, who died of strangulated umbilical hernia. There was scarcely a convolution in either hemisphere which did not at some point show foci of cicatricial puckering. The associated reduction in size of the brain was so great that the weights are worth recording, encephalon, 970 grammes; right hemisphere, 402 grammes; left hemisphere, 402 grammes; cerebellum with pons and medulla, 138 grammes. The skull was very thick and the frontal bones rough internally. Calcification of arteries was general and extreme.

Case 4.—A female, aged 65 years, suffering from dementia. The brain was small (1,070 grammes), and, in addition to senile changes, presented withering of the gyri bordering the horizontal limb of the intraparietal sulcus and the second frontal sulcus in the right hemisphere. The case was unusual in that the change was unilateral. The subject was stout and well-nourished, the larger arteries were very calcareous, and the kidneys in a state of senile arterio-sclerotic fibrosis.

Commentary.

As three of these subjects were women, we may say that the female sex is disposed to the disease more than the male. Age also seems to bear an influence, because, although the man was but 24 years old, all the women had reached senility. The relation between the disease and an affection of the arteries is of greater importance. In the young subject the influence of syphilis could not be excluded, and in the remaining cases the arteries exhibited a degree of atheroma and calcification such as is not often seen even in cases of advanced senility; and, as I have already indicated, the distribution of the cerebral disfigurement favours the suggested relation to syphilis. At the same time, when we remember that rupture and thrombosis of such vessels are frequent in the aged, and particularly in the aged insane, it is singular that there was no gross lesion in any of these cases; and equally strange that in one case alone we found that dilation of the perivascular channels and those small scars in the central nuclei and white substance which we associate with degenerated vessels.

We will now enquire into the nature of the process, and here we shall be helped by the microscopic appearances.

Microscopic Examination.

Having made horizontal as well as transverse sections of many affected gyri, I have come to the conclusion that the change is attributable to a discrete occlusion of numerous

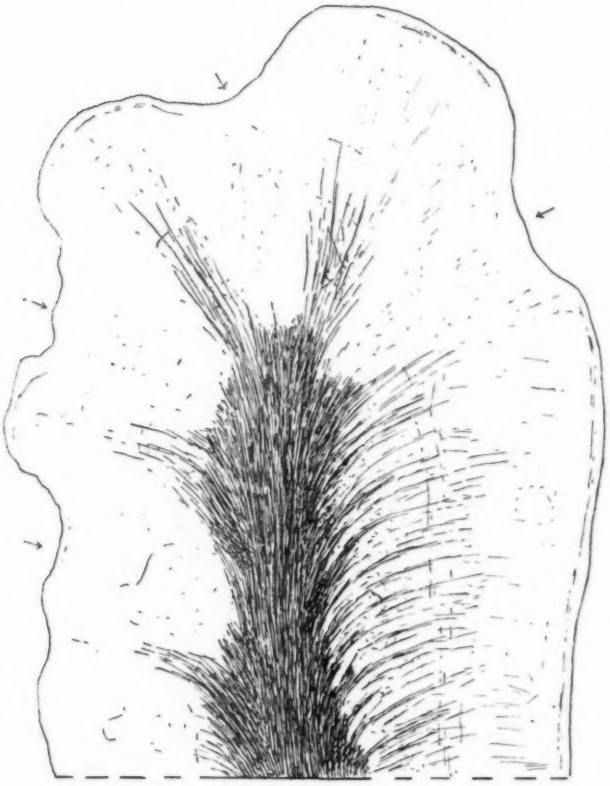


FIG. 17.

Cerebral Arterio-Sclerosis.

A semi-diagrammatic representation of a transverse section of one of the affected gyri, stained for nerve fibres. Along the margin are indentations which correspond with the pits seen before section. Beneath these the cortex is wholly denuded of nerve fibres and nerve cells and converted into glial tissue: elsewhere it is healthy. × 80.

cortical arterioles. First taking the appearances on transverse section, the cortex is divided into a series of healthy and diseased compartments; strips of substance entirely bereft of nerve fibres and cells, and composed of glial tissue only, alternate with strips wherein the nerve cells and fibres, although distorted by cicatrisation, are preserved; and it is interesting that each sclerosed strip lies immediately below one of the surface pits. Turning to the horizontal sections, the fields of sclerosis seen before as strips now appear as islets occupying about half a low power field of the microscope, most of them isolated and circular, but some oval and joined to neighbouring islets by a linear band of glial tissue. These islets are composed solely of fine glial fibres, and appear to be non-vascular; evidently by contraction they have drawn on the surface and caused the pitting which is a feature of the lesion. At the edge of each islet, in the adjoining healthy substance, one or more blood-vessels run, and also as a result of cicatrisation these are dilated. Elsewhere the vessels show hyaline degeneration and general senile changes. There is no indication of cyst formation, nor can hæmoglobin crystals be found.

To explain these microscopic appearances, we can only suppose that each strip or islet of sclerosis represents a field of substance originally supplied by a cortical arteriole now for many years occluded. Not to discover the occluded artery running down the centre of each strip is no proof against this origin, because time has converted the vessel into connective tissue, but it is hard to understand why some arteries should be selected for stoppage and others left patent.

In conclusion, gyral arterio-sclerosis with atrophy and pitting is a disease chiefly confined to aged dements with diseased arteries, it attacks the cortex in patches, and apparently is the outcome of a discrete occlusion of cortical arterioles.

Chapter 8.—Colloid Sclerosis.

An affection of the blood-vessels is the principal factor in this form of sclerosis; glia-cell proliferation participates only to a minor extent. The condition is rare; for several

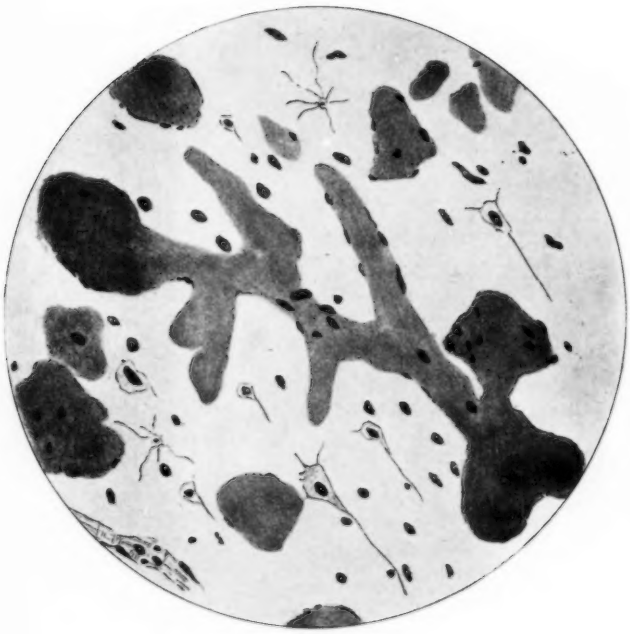


FIG. 18.

Colloid Sclerosis.

A microscopic drawing to indicate the size and shape of the colloid masses. The form of the main mass proclaims that it is an altered vessel. The drawing is taken from the level of the large external pyramidal cells. × 250.

years it was our routine practice at Rainhill to examine microscopically some part of the cerebral cortex in the case of every patient who died, and, with my later experience added, I have now notes of the inspection of more than 500 brains. In one case alone have the appearances I am about to describe been observed.

The subject was a man, aged 38 years. He presented the classical signs of general paralysis, and this combined with tuberculosis of the lungs to cause his death. As indicating general paralysis the brain was greatly wasted (weight of encephalon 1,162 grammes), the pia-arachnoid membrane was thick and opaque, the ventricles were dilated, and the ependyma was granular; and as the feature of special interest we found all the gray matter of the brain, including the cortex of both cerebrum and cerebellum, and the substance of the basal nuclei, greatly increased in firmness and abnormally yellow. Of course, it is the rule in general paralysis for the cortex to be unduly firm, but in this case the induration was profound, declaring itself not only to the fingers but to the knife.

The lungs provided examples of acute "pneumonic" phthisis, and, as proving the rapidity of its progression, there was no ulceration of the intestines.

The remaining organs were free from gross disease, and I must note specially that they were not lardaceous.

Microscopic Examination. (Fig. 18.)

In sections of the cortex and basal nuclei an abundance of large, semi-transparent, almost homogeneous masses immediately arrests attention; a few of these are cylindrical, but the majority are round, and for the latter 35 μ is an average diameter. Occasionally what appear to be concrete masses, giving a transverse measurement of about 180 μ, are seen. Many of the masses contain a few nuclei like those in vessel walls, but in other respects they are structureless. They present no concentric markings. They are almost transparent, and in the presence of most dyes retain their natural yellow tint; with methyl violet, however (in Weigert's stain for neuroglia), with hæmatoxylin,

and with carmine, they stain intensely. With ordinary solutions of methyl violet a faint pink tint suffuses the intense violet colour, but, as proving that the reaction is not that of amyloid tissue, the masses neither turn brown with iodine nor blue with iodine and sulphuric acid. In the case of the basal nuclei the masses are more numerous in the caudate and lenticular bodies than in the optic thalami, and in the cortex they distinctly favour the walls and floors of sulci. The white matter is not deeply invaded.

Notwithstanding that this change cannot be shown in every section, there is no doubt that the masses are directly related to, indeed, represent, blood-vessels. On the question whether the process is a degeneration or an infiltration it is hard to pronounce an opinion, but, judging from general appearances, and particularly from the way in which the material follows each vessel in the form of a confluent mass, I prefer to think that we have to deal with an infiltration or a precipitation in and around the tissue elements rather than a degeneration. The change produces great thickening of the vessel wall, and here and there remarkable bulgings or buds (*vide* fig. 18), which are further curious in staining more intensely than the rest of the vessel. The isolated masses represented in the drawing are similarly thickened portions of surrounding vessels on partial section.

As to the nature of the material, I have little hesitation in declaring it to be colloid; it could only be confused with hyaline matter, but not if it be remembered that tissues altered by hyaline degeneration do not stain with methyl violet. Also I believe that the change is identical with that seen by Alzheimer in one case of general paralysis and in one of epilepsy.

Reference.

Alzheimer. "Die Colloidenentartung des Gehirns." *Archiv. f. Psychiatrie*, 1898, p. 18.

Chapter 9.—Giant Cell Sclerosis.

Perhaps more commonly than we imagine sclerosis manifests itself in a heterotopic anomaly of the nervous system in which a collection of giant nerve cells is an important

FIG. 19.

Giant Cell Sclerosis.

A camera lucida drawing showing two of the pallid giant nerve cells, with eccentric nuclei, which occupy the mass. Two capillaries and some nuclei of the neuroglia are included in the figure.

Stain, Thionin. Magnification × 300.

constituent. I have seen one case, an epileptic woman, aged 23 years, with various physical stigmata of degeneration, and a family history disposing to nervous disease and insanity.

In the second temporal convolution of the left hemisphere, four centimetres behind the tip of the lobe, imbedded in the white substance immediately below the cortex, was an indurated mass of the same colour as surrounding parts, and about the size of a hazel nut.

The microscopic sections I have prepared are occupied by numbers of giant multipolar cells, similar in shape and equal in size to those in the precentral gyrus (motor area), but their processes, which are long, point in all directions; their protoplasm is pallid, contains no Nissl bodies and is sometimes vacuolated, and the nucleus, small in proportion to the size of the cell, is frequently eccentric. Other nerve cells dotted about are small and polymorphous. The field is rich in nuclei of the neuroglia, and is interlaced by abundant fine capillaries. The overlying cortex appears to be healthy. (Fig. 19.)

I am conscious of transgression in including this condition in the category of sclerosis; still the giant cells are reminiscent of those seen in cases of tuberose sclerosis, and it was by the induration alone that the growth was detected. If it should not be accepted as a form of sclerosis, the name "glioma gangliocellulare," not so aptly applied to tuberose sclerosis, might meet the case.

Chapter 10.—Other Forms of Sclerosis.

There are several other forms of cerebral sclerosis, but being of common occurrence and having a known pathology they require only brief mention.

(*a*) *Sclerosis in General Paralysis of the Insane.*

We are familiar with the cerebral induration of general paralysis, and in the majority of cases do not err in ascribing it to the proliferation of glial tissue, and the universal thickening of vessel walls running in company with the neuronic degeneration characteristic of this disease.

(b) Cerebral Sclerosis in Senility.

As in general paralysis, so in senility, neuronic decay, vascular disease and glial proliferation combine to cause a general increase in the firmness of the brain.

In special cases, localised induration attended by extreme wasting of gyri occurs, and may be explained by atheromatous narrowing of the lumen of special arteries to the parts, whereby the blood supply, without being quite cut off, is much diminished, so aggravating the ordinary process of senile decay.

I have seen several cases in which the tips of the temporal lobes and the gyri on the convex face of the frontal lobe have been selected for affection in this manner.

(c) Sclerosis of the Cornu Ammonis in Epilepsy.

Although I have examined a number of brains from cases of epilepsy, I have found no support for the statement of early writers that sclerosis of the cornu ammonis is a common feature in this disease. Clothed by a dense, felted lamina medullaris externa, or zonal layer, and strengthened by radiating fasciculi of long and stout medullated nerve fibres, the cortex of the cornu ammonis, or gyrus dentatus, indeed, of the whole hippocampus, including the lobus pyriformis, is structurally firmer than other parts of the brain, and often feels much indurated, but not more often in epilepsy than in other diseases.

(d) The Effects of Cerebral Softening and Hæmorrhage on Surrounding Parts.

There is no doubt that the puckering and induration affecting gyri along the borders of a patch of ordinary embolic or thrombotic softening, or the parts around a hæmorrhage, are due to the severance and decay of internuncial neurons and the subsequent proliferation of neuroglia brought about by the arterial disturbance.

I have already mentioned that such cases have proved of great use to me in studying morbid conditions of the neuroglia, and there is no occasion to enter further into their histology.

(*e*) *Microgyria in Idiocy.*

In addition to the microgyrous conditions affecting idiots, described in foregoing sections, there is one which is very common, and though more frequent in the parietal and occipital lobes than elsewhere, it is not restricted to any particular part of the brain. The diseased area varies in extent, and is represented by a small nucleus of puckered and contracted, or wholly-destroyed, gyri, surrounded by others which are attenuated and sclerosed, but not deformed. There may be more than one lesion, and in any case considerable cerebral deformity and asymmetry results.

I refer specially to this condition in order that I may protest against the view that such areas are manifestations of some developmental error. I have seen many cases, and in all the distribution of the lesion and the constant signs of post-necrotic destruction in the centre of the area suggested a vascular origin, namely, embolism or thrombosis, at birth or soon after, of the artery leading to the part.

(*f*) *Cerebral Sclerosis in Syphilis.*

More or less widespread sclerosis of the brain has been reported in cases of congenital syphilis, but I myself have not seen an instance of the affection. In cases of gummatous subdural growths, however, arising in adults, I have observed infiltration and induration of the subjacent brain substance to a depth of several millimetres; and in other cases of syphilis, also in adults, I have noticed sclerosis and attenuation of gyri, particularly those of the frontal and temporal lobes, which I have ascribed to partial closure by syphilitic endarteritis of the supplying arteries, a condition which I have considered as akin to that sometimes seen in the brains of aged individuals with atheromatous vessels. Clinically, in such cases, the diagnosis of syphilitic pseudo-general paralysis has been sometimes made.

(*g*) *Disseminated Sclerosis.*

To complete the list of forms of sclerosis I have only to name disseminated sclerosis (sclérose en plaques) and military sclerosis, and mention that I have nothing to add to the descriptions of these conditions given by others.

THE CLINICAL HISTORY AND *POST-MORTEM* EXAMINATION OF FIVE CASES OF MYASTHENIA GRAVIS.

BY E. FARQUHAR BUZZARD, M.D., M.R.C.P.,

Assistant Physician to the National Hospital for the Paralysed and Epileptic, to the Royal Free Hospital, and to the Belgrave Hospital for Children.

With Five Figures.

In a paper which was read before the Pathological Society of London I have already given a short summary of the histological findings in the five cases of myasthenia gravis which form the subject of this communication, but it appears to me desirable that a full account of these cases should be placed on record, inasmuch as they present features which are not only of pathological but of clinical interest.

The object of the present paper may therefore be regarded as two-fold. In the first place it will draw attention to some striking clinical phenomena occasionally occurring in this disease, and in the second place it will serve to propagate the view, which my experience has caused me to hold, that there are constant morbid changes associated with myasthenia gravis.

My best thanks are due to Dr. T. Buzzard, Dr. Ormerod, Dr. Head, and Dr. Wall, for their kind permission to make use of the clinical notes on the cases under their care.

Case 1.—A. J., aged 41, was admitted into the National Hospital under the care of Dr. T. Buzzard on November 3, 1903. His family history was too vague to be of importance.

His previous health had been good; but at 16 he contracted gonorrhœa, followed by no evidence of a sore or of secondary syphilitic symptoms. In 1892 he injured left eye and suffered from monocular diplopia for eight years. Moderate drinker of beer; no spirits. Occupation for twenty-one years had been that of a stone-grainer. Married nineteen years; fourteen children, of whom six died in infancy and one was stillborn.

PLATE I.

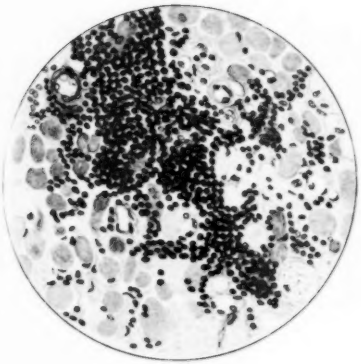


FIG. 1.

Section of inferior rectus muscle of Case 1, typical of lymphorrhages in ocular muscles.

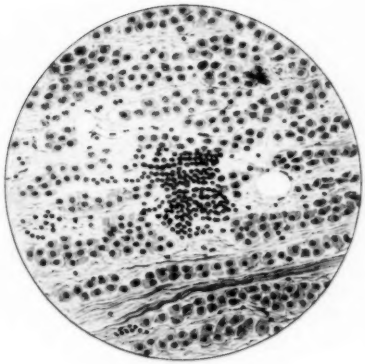


FIG. 2.

Section of adrenal gland in Case 4. A small lymphorrhage in the cortex of the gland.

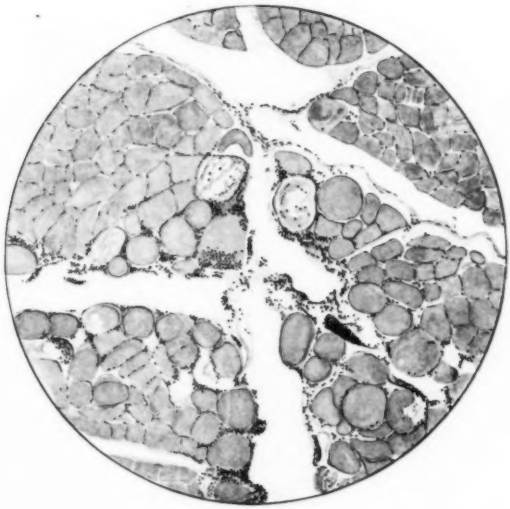


FIG. 3.

Section from triceps muscle of Case 5, showing marked changes in muscle fibres, some of which have been invaded by the cellular exudation.

Present illness.—For three or four years the patient had been obliged to lift his upper eyelids with his fingers when reading for any length of time. In other respects he had been well until March, 1902, when he noticed a feeling of heaviness in the right leg, which became easily tired. A month later he experienced an aching pain, first of all in the right foot, then in the left shoulder, and later all over the body, which would come on after he had been up for a couple of hours and remain until he turned in for the night. More recently he had been unable to walk more than fifty yards, after his work, without resting. For two or three months he had noticed a difficulty in swallowing, the bolus of food lying at the back of the throat and tending to get into the nasal passages. During the same period saliva would collect in his mouth and shortness of breath and difficulty in articulation would come on rapidly after a short conversation. At times his voice failed altogether, and his speech became unintelligible. He had lost two stone in weight during the previous year.

Condition on admission.—The patient was spare, but muscular, somewhat pale and tired-looking, and his movements sluggish and feeble. His forehead was almost constantly wrinkled in the effort to overcome the ptosis of both upper eyelids. As a witness he was bright and intelligent, answering questions readily and clearly. His appetite was good and he slept well.

With the exception that his heart sounds were somewhat feeble, all the internal viscera appeared to be healthy. There was no evidence of glandular enlargement in the mediastinum or elsewhere.

The examination of the blood showed 3,496,000 red corpuscles and 8,000 white corpuscles per cubic millimetre; Hæmoglobin 60 per cent. There were no abnormal forms of red or white cells, and the different varieties of the latter were present in the usual relative proportions.

Smell, taste, and hearing were perfect.

Sight $\frac{6}{9}$ with both eyes. Visual fields were normal. The fundus of each eye was healthy in appearance.

All ocular movements were very limited in range, the horizontal being restricted to about one-sixth and the vertical to about one-quarter inch.

The axes of the eyes were parallel and diplopia was not complained of. Pupillary reaction to light and accommodation was healthy. Marked ptosis was present on both sides. No nystagmus was observed.

Fifth nerve.—All movements of the jaw were performed with

fair power. Opening and shutting the mouth was repeated 594 times before the patient was tired. On the other hand 45 momentary applications of a mild faradic current wore out the contractility of the left masseter. There was no alteration of sensibility in the skin of the face.

Seventh nerve.—All facial muscles were more feeble than normal, but the orbiculares palpebrarum and oris markedly so. The orbicularis palpebræ did not contract to a faradic current. The left zygomatics were exhausted by 50 applications.

The ninth and tenth nerves.—Deglutition was always difficult, even with the softest food, fragments of which were very apt to pass into the nose.

Liquids were swallowed more easily. Phonation tired rapidly, and might be absent altogether in the evening.

The palate was flaccid and moved very little, either on phonation or on reflex stimulation.

Twelfth nerve.—The tongue movements were fairly good, and it was not noticeably wasted. It was protruded ninty-one times before being tired.

The neck.—Patient could not raise his head from the pillow. When sitting up the head would fall forwards unless supported.

Upper extremities.—Movements performed by the muscles of the shoulder girdle were all feeble. The biceps was still more feeble, while extension of the forearm by the triceps could scarcely be carried out. Wrist movements were rather better, but both grasps were poor. All movements of the fingers could be made, but were easily resisted. There was no wasting of any muscle.

Trunk.—Patient could not sit up even with the help of his hands, but the abdominal muscles could be felt to contract in the effort. When in the sitting position the back assumed a round kyphosis, which could not be voluntarily straightened.

Respiration was partly thoracic and partly diaphragmatic, but shallow in type.

Lower extremities.—All muscles were well developed and their power much better than that of the muscles of the upper extremities. Extension of the right ankle was the weakest movement. The gait was good and no dragging of feet was noticed.

The co-ordination of all limbs was normal, and the sense of position accurate. No tremors were observed. Romberg's sign was not present.

Sensory system.—Aching pains in various parts were complained of, especially after movement. Attacks of sharp pain

occasionally affected the inner side of his arms and his back. There was relatively diminished sensibility to light touches and to pricks over the ulnar aspects of the arms.

Reflexes.—The Jaw-jerk was present. Triceps and supinator-jerks were not elicited. Knee- and ankle-jerks were brisk. Epigastric, hypogastric and cremasteric reflexes were present. Plantar reflexes were of flexor type. The knee-jerk was not exhausted by 300 consecutive stimulations.

Electrical reactions.—To galvanism all muscles reacted normally. To faradism the following muscles reacted well at first, but were exhausted by varying numbers of applications.

Left sternomastoid	... 46	... Right	50.
,, trapezius ...	... 14	... ,,	14.
,, supraspinatus	... 16	... ,,	31.
,, deltoid ...	... 52	... ,,	56.
,, extensor digitorum	114	... ,,	96.

January 29, 1904.—The patient has been suffering greatly with shooting pains, chiefly in the lower extremities, and from one or two attacks of respiratory failure, in which he was markedly cyanosed. The right knee-jerk is now much diminished and exhausted by six taps. The left is exhausted by twelve taps.

January 31.—Much weaker lately. Yesterday the temperature rose to 102° without obvious cause. Occasional profuse sweats are noticed.

The special senses are unaffected.

The patient has still marked ptosis which varies considerably, and is generally more marked in the evening than in the morning. There are practically no vertical or outward movements of the eyeballs, and inward movements are very limited. A week ago the only movement possible was a slight degree of conjugate movement to the left. Pupils react well. Chewing food causes rapid exhaustion of the jaw muscles. All facial movements are very feeble. He cannot fully close the eyes or whistle. The face is very expressionless. In smiling the mouth is merely elongated and its angles slightly raised. The muscles do not appear to be wasted. Fluid tends to run away from the corners of the mouth, and solid food collects between the teeth and cheeks. Regurgitation of fluids through the nostrils takes place occasionally. Swallowing of solids on some days is very difficult, and attended by choking and coughing. Articulation and phonation are easily exhausted.

The tongue is large and flabby, and all movements are readily tired on repetition.

There is no wasting of the muscles of the extremities, but they are flabby and toneless.

Movements of the neck are fairly good, but he is unable to hold his head erect for any length of time when sitting up. Patient cannot extend the upper limbs in front of him for more than a minute, and the left fails before the right. The grasps are feeble, but the relative strength of the movements varies considerably from day to day.

Respiration is chiefly diaphragmatic, and during the attacks of dyspnœa from which the patient occasionally suffers, the thoracic movements are very feeble and shallow. The act of coughing is poorly performed. No special weakness of abdominal or spinal muscles is observed.

Patient cannot raise either extended leg from the bed, nor can he extend the knees against gravity. Other movements of the lower limbs are relatively stronger. There is no inco-ordination, tremor or fibrillation observed in any limb.

All voluntary muscles are easily exhausted by rapid repetition of action, and there is analogous exhaustion of many of the weaker muscles by rapidly repeated faradic shocks. For instance, the biceps on each side is completely exhausted by sixty shocks, and the triceps by thirty stimulations. On the other hand, the pectoralis major was not completely put out of action by one hundred faradic shocks. Even when the muscles are completely inactive to faradism they respond briskly to galvanism. An effort to exhaust the muscles by direct mechanical stimuli was not successful.

Subjective sensations are divided by the patient into three classes: (1) Dull aching pains, chiefly in shoulders and back of neck; (2) a general tired feeling and a sensation of tightness and stiffness about the knees; (3) shooting pains of a sharp stinging character which dart from place to place in the lower limbs.

On testing there is considerable relative anæsthesia and analgesia along the ulnar borders of the arms extending over the ulnar half of each little finger. On the trunk the sensory loss involves a definite area between the second costal cartilage and a line about 1 in. below the nipples. There is also a slight degree of analgesia on the peripheral parts of both lower extremities. Muscle pain sense is also reduced in the legs, but there is no loss of sense of position in any limb.

Reflexes are in the condition mentioned in the previous notes.

The sphincters are unaffected.

April 11.—His condition remained unaltered until about ten day sago, when it became considerably worse. On some days the patient has scarcely been able to swallow at all, even his breakfast, and respiration has been difficult and associated with cough. Only a little pale mucus is expectorated after great effort, owing to the feeble nature of the cough. No abnormal physical signs are detected in the lungs. The urine is normal. The ptosis and ophthalmoplegia are much as before, but the pupils are smaller and react rather sluggishly to light. Mastication and jaw movements are very poor; towards evening the lower jaw drops, and has to be supported by the hands during conversation. There is some anæsthesia and analgesia over the central part of the face, including the nose.

Articulation and phonation are feeble.

The arms are much more weak; the patient can extend neither in front of him. Full closure of the fist is impossible. Abdominal muscles are definitely affected. The lower limbs are much as before, but more easily exhausted.

Subjective sensations remain as before, except that the shooting pains are more severe.

Analgesia is more intense and extensive than at the time of the last note. The ulnar half of each arm and both little and ring fingers are affected. On the trunk there is almost complete analgesia between the second costal cartilage and a level about an inch above the umbilicus. Analgesia is also more extensive on the lower limbs.

There is complete loss of sensibility to cotton wool on the whole of the upper extremities excepting a narrow strip along the radial border and thumb. The same condition obtains from the second costal cartilage to the umbilicus, and to a less extent below that level.

On the legs there is almost complete loss to the same test, but this fades off above the knees. The reflexes are as before, except that the abdominal and epigastric are not now obtained.

The fingers are now pointed and the skin over them thin, shiny and glossy.

The patient grew worse and had several attacks of respiratory failure, in one of which he died on April 26, 1904.

The autopsy was performed ten hours after death, when *rigor mortis* was well marked. The body was poorly nourished, but not emaciated. Nothing abnormal to the naked eye was observed in the course of removing the brain,

by their size, and by the fact that the nucleus is generally round or slightly oval and surrounded by an extremely narrow belt of protoplasm. In the second place they have infiltrated the tissues in the same way as red blood corpuscles do in the case of a capillary hæmorrhage, and are not, as a rule, associated with obvious changes in the surrounding structures, inflammatory or otherwise (Plate I., fig. 1).

In longitudinal sections similar lymphorrhages were met with, and some of these measured as much as ·3 mm. in length. Here, again, the cells were seen to lie in the spaces between the muscle fibres and not to invade them.

Every now and then a capillary vessel was observed running through the cells, generally empty but occasionally containing red corpuscles. Passing from the consideration of these lymphorrhages the condition of the muscle fibres next claims our attention. A careful comparison of the fibres in this case was made with those in similarly prepared sections from a normal ocular muscle, with rather indefinite results owing to the great difficulty in forming an opinion. It may be stated generally that the large majority of fibres were of normal size and appearance, but that possibly there was a greater variety in calibre than is seen in the healthy muscle. There is certainly not any marked increase of nuclei nor proliferation of connective tissue.

No abnormality could be detected in the nerve bundles or in the blood-vessels.

The sections stained by the Weigert-Pal method gave a beautiful picture of nerve fibres apparently well myelinated as far as their muscular connections.

Cardiac muscle.—The preparations of cardiac muscle stained by logwood and eosin were of perfectly normal character and free from any lymphorrhages.

Skeletal muscles.—Portions of the biceps femoris, vastus internus, tibialis anticus, and triceps muscles, were hardened in formalin and cut in paraffin and celloidin. A large number of sections were stained by the logwood-eosin method and examined.

spinal cord, and various nerves and muscles. The left eyeball was removed with the optic nerve and ocular muscles attached.

The thoracic organs were healthy in appearance, and only slight traces of the thymus gland could be detected in the fatty tissue of the superior mediastinum. The thyroid gland was well developed. The spleen was natural except for the presence of two small calcareous lumps in its substance. The pancreas, liver and kidneys were normal. The adrenal bodies were not obviously diseased. There were no enlarged peritoneal glands. Both scrotal sacs contained hydroceles with clear fluid—the testicles were free from disease.

Microscopical.

Ocular muscles.—The muscles attached to the left eyeball were hardened in formalin and cut, some in paraffin, but the majority in celloidin, which gave much the better results. Longitudinal and transverse sections were made of each muscle. Most of the sections were stained by hæmatoxylin and eosin, but a few were stained by the Weigert-Pal method. It is unnecessary to detail the changes found in each muscle, as they were more or less the same, and the inferior rectus may be taken as a type of the others. Transverse sections across the body of this muscle, stained by the logwood-eosin method, presented unusual appearances, even with a low power, owing to the presence of three or four darkly-stained clumps of cells. These clumps were of various sizes, the largest measuring about ·2 mm. by ·15 mm. Under higher powers it was seen that these unusual appearances were due to the presence of a large number of cells, indistinguishable from the ordinary lymphocytes of the blood, lying scattered between the muscle fibres, nerve bundles and blood-vessels. Since these cell-clumps are characteristic and present in many parts of the body in this disease, I have proposed, for the sake of brevity, to denote them by the term "lymphorrhage." This name is chosen for two reasons. In the first place the cells are, as has been said above, indistinguishable from lymphocytes

The ventral half of the crural region of the brain-stem, including the outgoing third nerves, was also examined by the Busch method with negative results.

A muscular branch of the oculomotor nerve was stained by the Weigert-Pal method and the fibres presented a perfectly healthy appearance.

The left optic nerve was cut longitudinally and transversely, and sections of it stained by Weigert-Pal and by logwood and eosin. Nothing abnormal was detected.

Spinal nerves.—A short length of the left ulnar nerve, taken from the region of the elbow, was stained by Busch's method and teased. No evidence of degeneration was observed in any of the fibres.

Another portion of the same nerve was embedded in paraffin and stained with logwood and eosin, but nothing abnormal was seen in the sections.

A piece of the anterior crural nerve was stained by Busch's method and cut in celloidin. No degeneration was found. Transverse sections of the sciatic nerve were stained by logwood and eosin and appeared to be healthy in all respects.

Spinal nerve roots.—The first dorsal anterior and posterior roots of one side were teased in Busch's fluid, but no pathological changes were detected. The posterior root of the opposite side with the ganglion attached was cut and stained with logwood and eosin. The root fibres were healthy in appearance, but owing to faulty fixation I do not feel inclined to express any opinion on the condition of the ganglion cells. In this ganglion and in several others from the dorsal and lumbar regions there were present a few small collections of lymphocytes scattered between the cells. As far as I could judge they were similar to the lymphorrhages in other tissues, although generally smaller.

Central nervous system. — The Busch, Weigert-Pal, Nissl and logwood-eosin methods were employed for the examination of the central nervous system after it had been hardened in 5 per cent. formalin. The parts examined included the left motor cortex, the oculomotor region of the brain-stem, the pons, medulla and various levels of the

Some longitudinal sections of the vastus internus showed fairly numerous lymphorrhages differing little from those seen in the ocular muscles. Some of them, however, were rather more extensive, from ·5 to 1 mm. in length. The cells lay quite free between the fibres, and there was no evidence of reaction in the latter. The sections taken from the other muscles did not present lymphorrhages, but it is hardly necessary to say that this fact does not signify an absence of lymphorrhage from the muscles.

Here, again, it was obligatory to investigate carefully the muscle fibres. In longitudinal sections the transverse striation was generally well marked and the fibres appeared healthy. In transverse sections it was noticed that a certain proportion of the fibres differed from their neighbours in two respects. In a transverse section of a normal skeletal muscle the fibres present polygonal shapes and fit together in a mosaic-like pattern. In the sections under consideration a number of fibres were rendered conspicuous by their rounded and non-angular contour and sometimes by their greater size. The same fibres were often still further differentiated by the fact that their protoplasm was more homogeneous and of a paler and more yellow hue than that of their healthy neighbours. Such variations from the common type are occasionally met with in presumably normal muscles, but are not nearly so numerous as in the sections obtained from this case and, as we shall see later, from other cases of myasthenia gravis. In all other respects the muscles appeared to be healthy, and sections stained by Busch's method showed no evidence of fatty change.

Cranial nerves.—A portion of the left trigeminal nerve close to its origin from the pons was stained in Busch's fluid, teased and examined microscopically. Not a single degenerated fibre was found. A portion of the oculomotor nerve, close to its central origin, and one of its muscular branches were treated in the same way and with the same result.

The right trigeminal nerve was stained by Busch's method and cut in celloidin; the sections showed no degeneration.

cord. With the exception of a few recent capillary hæmorrhages in the gray matter of the cervical cord the results were entirely of a negative character. Not a suggestion of early tabetic changes could be detected by the Weigert-Pal or Busch methods and the ganglion cells generally were of healthy character, as portrayed by Nissl's stain.

Liver.—Sections of this organ showed small scattered patches of fatty degeneration. Here and there were seen a few collections of lymphocytic cells resembling the lymphorrhages seen in the muscles. These appeared to be associated in most cases with a small intralobular capillary and sometimes a few of the neighbouring hepatic cells had undergone degenerative changes. In other respects the sections appeared healthy.

Adrenal bodies.—Sections from these glands revealed perfectly normal structures except for the presence of a few lymphorrhages. One or two larger ones were situated in the medullary part of the gland and a few smaller ones in between the cell groups of the cortex. It was noticed that the neighbouring capillaries were often engorged.

Pancreas. — Microscopical examination of this organ revealed no abnormal features.

Kidneys.—As far as the glomeruli and tubules were concerned these organs seemed to be healthy. Now and then there appeared to be an unusual number of small round cells lying between the convoluted tubules. The aspect produced was different from that of the lymphorrhage in other organs because the cells were not lying together in rounded clumps but spread out between the tubules. It is difficult to express an opinion as to the abnormality of this appearance, and I prefer to leave the question open.

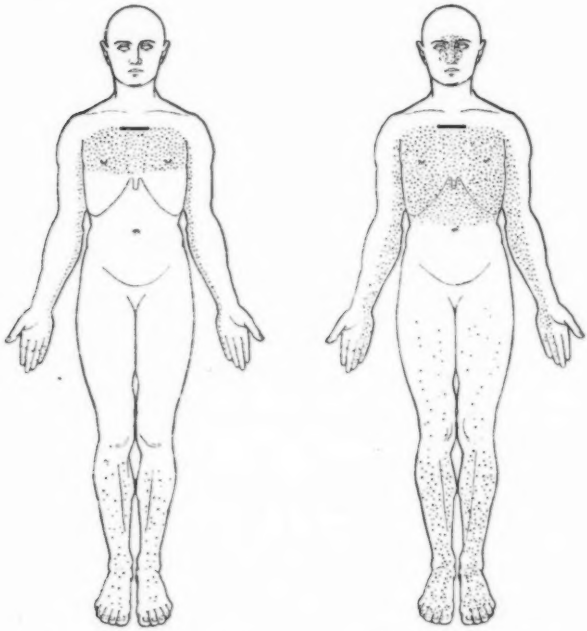
Testicle.—Sections of this organ presented no unnatural feature.

The thyroid gland, pituitary body and spleen were all healthy as regards their histological appearance.

Thymus.—Report by Dr. Dudgeon. The fibrous tissue in which the scanty islets of thymus tissue are to be seen consists of very dense tissue without any nuclear marking

in places. The cortex of the gland cannot be distinguished from the medulla. Many of the concentric corpuscles are very large and calcified in great part.

Case 2.—A Russian Polish woman, aged 28, was admitted to the National Hospital on October 8, 1902, under the care of Dr. Ormerod.



Analgesia, January 31, 1904. Analgesia, April 11, 1904.

Family history.—Mother died of consumption. Father is alive and healthy. Five brothers and sisters are alive and healthy. There is no history of any similar condition in any relation.

Previous health.—Health was good with the exception of measles until the onset of present illness. Married eight years, but has never been pregnant. Husband is now 50 years of age and had children from his first wife. Patient's food has been of the ordinary character, and she has abstained from alcohol for some years.

Speech is normal. Articulation begins well, but soon tires. After frequent repetition the word "grub" becomes "grum," and by this time the patient is unable to blow out the cheeks without air escaping.

The pupils react to light and on accommodation, and this reaction was not exhausted by frequent stimulation or effort.

The muscles of the limbs exhibit diminished power generally, and this defect becomes much more marked on exertion, not only in the muscles exerted but in those of other parts. It was noticeable too that, after the limbs had been in a state of activity for a short time the ptosis of the eyelids would become more severe. The respiratory movements were of normal type and depth.

Sensation.—The patient complains of pain of two kinds: (1) general aching and stiffness, especially after exertion; (2) sharp intermittent pains as described above. On testing, cutaneous sensibility appeared to be perfect, except in a small area over the left shoulder, where there was relative anæsthesia and analgesia. It should be mentioned that the testing of sensation in this patient was unsatisfactory owing to her mental attitude.

Reflexes.—All deep reflexes were brisk and not exhausted by repeated stimulation. The corneal and abdominal reflexes were brisk, and plantar responses of the flexor type.

The sphincters performed their function in a normal manner.

Electrical.—The extensors of the left wrist were stimulated by repeated faradic shocks and completely exhausted in three minutes. At this moment very little voluntary power was left in the muscles, but a galvanic current produced a normal contraction with K.C.C. greater than A.C.C.

The left facial muscles were exhausted in ninety seconds, and on asking the patient to show her teeth no movement was obtained on that side of the face.

December 10, 1902.—General condition has improved, but strength varies much from day to day. The pains continue at times, and are not associated with any rise of temperature, but appear to coincide with increased weakness. There is now paresis of the right external rectus muscle and diplopia on looking to the right. The other movements are much as before.

Heart and lungs are healthy. There is no enlargement of thyroid, and the abdomen is normal on examination.

January 20, 1903.—Last night patient complained of great pain in her left leg. To-day she says that leg is weaker than the other, and this appears to be the case on examination.

Present illness.—Seven months ago patient began to feel pain in the shoulders, the arms and the legs and a sensation of pins and needles in the tips of her fingers. The pains were sharp and intermittent in character and were worse in wet weather. About the same time she complained of weakness in the arms, hands and legs. She continued for a month in this condition doing her housework, but always suffering and becoming weaker as the day went on.

Six months ago she experienced a sudden difficulty in talking during a conversation with a friend; she felt her mouth become stiff and her tongue immobile. About the same date she began to see double and to have a certain amount of dysphagia. The pains and weakness in the limbs continued and during the last few months her symptoms have become considerably worse. Lately she has found it difficult to prevent food coming back from her mouth through the lips, but has had no regurgitation through her nostrils.

Condition on admission. — Both upper eyelids droop and the lower lip is somewhat everted. Around the lips the skin is studded with beads of perspiration and the whole face is slightly flushed and pink in colour.

In smiling there is no elevation of the corners of the mouth, only a widening of the oral fissure and increased eversion of the lower lip. In voluntary movements of the face the action is slow and badly maintained. The patient is unable to whistle, but can blow out her cheeks. The attempt to close the eyes causes a movement of the feeblest character, especially on the right side. Elevation of the eyebrows is equally deficient.

The ocular movements are briskly and fully performed at first, but soon become partially exhausted. There is no nystagmus and at the present time no strabismus.

Opening and closing the jaws is well performed at first, but after twenty repetitions the observer can place his finger between the teeth and allow the patient to bite with impunity. The tongue movements are good at first attempts, but tire easily. The tongue itself is somewhat peculiar owing to its flabbiness, and to the presence of three linear grooves on its dorsal surface, one median and two about half way between the midline and the lateral edges.

The palate moves well on phonation and in response to stimulation, both sides being raised equally. Only on one occasion has the patient had any regurgitation of fluid through the nose.

about 2¾ ins. at its broadest level. Its shape was roughly that of a pear with a narrow stalk above and a bilobar gland below. The weight of the organ was 41 grammes, and its consistence was firm throughout. The glandular substance was surrounded by a small amount of fat which could be readily stripped off its surface.

The thyroid gland was felt in its usual situation and appeared to be natural in size, shape and consistence. It was not removed.

All the abdominal and pelvic organs were healthy except for a small cyst attached to the right ovary.

The various organs and tissues removed were hardened in 5 per cent. formalin.

After hardening the thymus was again examined and a section made through the middle of its broadest part. There was no evidence of necrosis or of malignant disease and the appearances suggested a simple hypertrophy of the gland.

Microscopical.

Central nervous system. — The Busch, Weigert-Pal, Nissl and logwood-eosin methods were utilised for the purpose of examining sections from the motor cortex, brain-stem, medulla and spinal cord, but the results in all cases were negative so far as the discovery of any pathological changes was concerned.

Peripheral nerves.—Sections from the ulnar and sciatic nerves were stained by the Busch and Weigert-Pal methods with similar results.

Skeletal muscles.—Portions of the trapezius, deltoid, triceps and erector spinæ muscles were examined microscopically after embedding in paraffin or celloidin. Only a very few lymphorrhages were found and these were of small size. Numerous fibres, sometimes singly and sometimes in groups, were seen in transverse sections to be rounded in outline, often slightly swollen, and to react quite differently to protoplasmic staining reagents. With eosin or fuchsin the sarcoplasm assumed a pale and sometimes a rather bright yellow hue, the contrast to the pink colour

There is no sensory loss.

There is dulness on percussion over the upper part of the sternum, and for about half an inch on either side of it. There is no tracheal tugging, and nothing to be felt in the episternal notch.

September 25.—Patient went to a convalescent home in June, and improved considerably during the first few weeks she was there. Five weeks ago she experienced a relapse, especially in swallowing and articulation. Since that time she has become gradually weaker and can now only swallow fluids and only talk for a very short time. She has suffered from sharp pains in the face, throat and neck. During the last ten days she has been unable to walk alone, and has had difficulty in breathing when lying down.

Physical examination reveals much the same as before, only the paresis is much more marked in the limbs and respiratory musculature. The knee-jerks can now be easily exhausted by repeated taps.

November 6.—The patient remained in practically the same condition, with variations, until to-day. This morning she seemed somewhat better than usual, but at 2 p.m. had a sudden attack of respiratory failure. When seen she was lying in bed with face, lips and extremities very cyanosed, and making feeble, shallow, gasping attempts at respiration. After artificial respiration had been performed, and a hypodermic injection of strychnine given, the patient recovered, but several attacks of the same character followed in rapid succession, and death took place at 3 p.m.

The autopsy was made four and a half hours after death, before *rigor mortis* had developed. The central nervous system, its meninges and enveloping bones, were all perfectly natural and healthy to the naked eye. The examination was limited owing to the wishes of the relatives, and only a few muscles and nerves were procured for microscopical examination.

The thoracic and abdominal organs were examined and removed through an abdominal incision. The heart and lungs were healthy. Lying in the superior mediastinum and loosely attached by its anterior surface to the posterior aspect of the manubrium sterni was a large thymus gland the vertical length of which measured $3\frac{1}{2}$ ins. and the breadth

of the normal fibres being a striking one. Sections stained by Busch's fluid also revealed the presence of these fibres which then assumed a darker brown colour than their neighbours.

Whether the stain used was eosin or Busch the homogeneity of the plasma was equally noticeable and longitudinal sections displayed the same features.

Cardiac muscle.—Sections from the left ventricular wall were stained with logwood and eosin and presented two points of interest. There were fairly numerous small lymphorrhages of a definite character, generally closely associated with capillary vessels. Except for the fact that the cells were not clumped so closely together, these generally resembled the lymphorrhages seen in other muscles. The second point to be noted was seen in a series of four sections which displayed a capillary blood-vessel engorged with blood and surrounded by a serous exudation of considerable extent. This exudation contained numerous lymphocytes but practically no polymorphonuclear cells and no red corpuscles.

Unstriped muscles.—Sections of the œsophageal wall showed no changes in the unstriped muscles.

Adrenal bodies.—Histologically these organs were healthy looking, except for the presence of lymphorrhages, which were numerous. They were found in the medullary part, in the cortex, and in the loose connective tissue of the capsule. One unusually large one in the lower layers of the cortex was traced through a number of serial sections and in each had a diameter of about half a millimetre. This one obscured and probably destroyed a considerable amount of the glandular structure, but many of the smaller ones caused little or no reaction in the neighbouring cells.

Liver.—A few sections of this organ stained by logwood and eosin showed the presence of a few lymphorrhages, the best marked of which lay in the centre of a lobule and measured not more than ·15 by ·25 of a millimetre. In other respects the sections were natural.

Kidney.—No lymphorrhages or other abnormal appearances were observed.

Spleen.—Healthy, the follicles being particularly well marked.

The pancreas, the pituitary body, and a bronchial gland were examined microscopically with negative results.

The thymus.—(Report by Dr. L. S. Dudgeon.) The gland presents a normal appearance under a low power of the microscope, and there is no evidence of fibrosis. The cortex and medulla are clearly differentiated, and the cellular constituents are of normal structure. There is, however, a point of great interest in the fact that, although the gland is enlarged and the structure is of normal appearance, yet there is a complete absence of eosinophile cells, such as are met with in the large thymus glands of children and young animals. These cells, which are often present in very large numbers along the septa and around the blood-vessels, are entirely wanting. The only condition in which I have found these cells to be few in number or absent, if the gland is enlarged, is in cases of hypertrophy of the adult gland. Many of the Hassall's corpuscles are degenerated. One or two of these contain calcareous masses which fill almost the entire corpuscle. Hyaline degeneration is also extremely well marked, and some of the cells have quite a clear centre surrounded by only a few cells at the periphery. Numerous hæmorrhages are present in the gland tissue and the small blood-vessels are very congested, a condition which is often associated with death from diseases accompanied by increase in intrathoracic pressure in young children.

Case 3.—N. S., aged 37, was admitted into the London Hospital, under the care of Dr. Head, on February 3, 1904.

Family history.—Her father is alive and healthy at over 60 years of age. Her mother is 59 years old and in good health except for varicose ulcers. Three sisters and two brothers are alive and well. Five brothers and sisters died before reaching 3 years of age; cause unknown. One brother died at 19, of diabetes. No history was obtained of any nervous disease in the family.

Previous health and habits.—Patient enjoyed good health, except for the ailments of childhood, until September, 1902, when she was laid up for a fortnight with inflammation of the lungs. She drinks about five small cups of tea daily, and never any alcohol.

Present illness.—At the beginning of October, 1903, the patient complained of some headache and vague pains, and noticed some "stiffness" of the eyelids on waking in the morning. During the following week she experienced double vision, and had to give up work. Drooping of the right eyelid was then noticed, as well as some difficulty in articulation. Improvement set in and continued until about a week after Christmas, when she appeared to catch cold. Articulation became more difficult, her lower jaw seemed to drop, and her head tended to fall forward. In spite of rest in bed her symptoms became worse, and towards the end of January dysphagia was observed.

Condition on admission.—The patient's complexion was rather sallow, but there was no abnormal pallor of the mucous membranes and no cyanosis. The facial aspect was peculiar owing to the bilateral ptosis and dropping of the lower jaw. Speech was a little indistinct, and in talking the lower jaw was supported by the patient's hand.

Vision was good and the optic discs and fundi healthy in appearance. The sense of smell was perfect.

The amount of ptosis varied; at times the upper eyelid covered the eyeball, but at others she was able to expose the lower half of the cornea. All external ocular movements were abolished, but the pupils were equal and reacted briskly to light and accommodation.

Sensation over the face was normal, but all movements of the jaw were markedly paretic.

The facial movements were so diminished as to render the physiognomy expressionless and flat. The orbiculares palpebrarum and oris were almost completely paralysed.

Hearing and taste were normal.

The palate moved quickly on phonation, but the movement was of small range and poorly maintained. Phonation was feeble and whispering in character.

The tongue showed no obvious atrophy, but was small and convex on the dorsal surface when protruded. After twelve attempts protrusion was so limited that the tip did not pass the teeth. A minute's rest sufficed to restore the original mobility.

The muscles of the trunk and limbs presented no wasting, no tremors, no fibrillary twitchings, and no spasticity.

The head fell forward unless supported, but, when support was given, lateral movements were freely performed. The sternomastoids responded briskly to the faradic current, but fifty short

PLATE II.

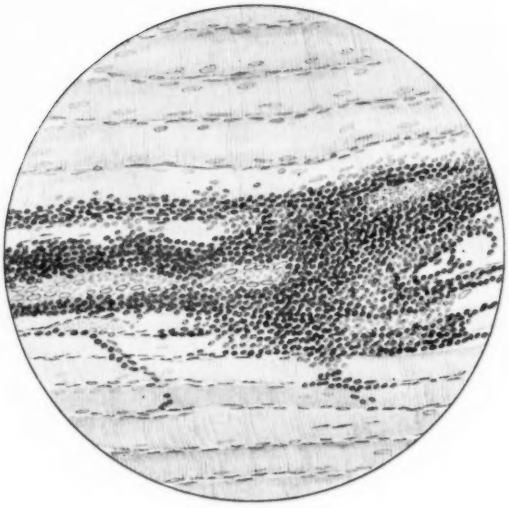


FIG. 1.

Section from the rectus abdominis muscle in Case 3, cut longitudinally and stained by logwood and eosin. Large focus of lymphocytes, healthy muscle fibres and, in the midst of the focus, a capillary vessel represented by a layer of endothelial cells.

FIG. 2.

Section from cardiac muscle in Case 3, stained by logwood and eosin. Many of the cells are here contained in capillary vessels lined by endothelial cells.

applications were sufficient to abolish the response. The response to galvanism was not interfered with.

The limb movements were carried out with fair power and co-ordination. The patient had only recently noticed any undue fatigue after walking.

Sensation everywhere was perfectly natural.

The knee-jerks were equal and brisk, and there was no ankle clonus. Plantar stimulation gave flexor responses on both sides.

The spine, sphincters and respiratory system were normal.

The heart was normal, pulse good, moderate tension, arterial wall not felt.

March 18, 1904.—Patient seems much worse, and muscular weakness is more marked.

She had two choking fits yesterday and one in the night.

April 15.—(Note by Dr. Head.) On the whole she is better, and has been up on a couch. The speech is distinctly nasal, and she holds her jaw with her hand when talking in order to bring the lips together. She cannot completely lift the eyelids nor close the eyes firmly. Profound ocular paralysis is present, especially in the left eye, where upward, external, and downward movements are impossible. There is slight power of internal movement. Slight degrees of upward, downward, and external movements are possible in the right eye, and internal deviation is about equal to that of the left. Pupils react normally. She cannot close her jaws, nor can she push her lower jaw forward or to either side. Movements of face can be made at command. The tongue can be protruded through the lips but not many times in succession. Palate movements are weak. Head tends to fall forward on the chest. Arm and leg movements are good. Sterno-mastoids still show the myasthenic reaction. Knee- and wrist-jerks are brisk and equal. Plantars give a flexor response. There is no sphincter trouble.

June 29.—Dr. F. Buzzard saw the case with Dr. Head. There is no impairment of resonance over the upper part of the sternum. There are no glandular enlargements. Thyroid region appears normal. The temporal muscles are definitely wasted.

July 1.—Differential count of white blood corpuscles made by Dr. Grünbaum.

Six hundred cells classified. Neutrophile polymorphonuclear, 73 per cent.; lymphocytes, 19 per cent.; hyaline, 4·25 per cent.; eosinophile, 3·25 per cent.; basophile, ·5 per cent.

July 11.—Knee- and wrist-jerks cannot be exhausted by frequent taps. The patient's condition remained much the same

although she lost weight and wasted considerably, until September 23, when she had some severe choking fits, became very dyspnœic, and died.

The autopsy was made twenty-four hours after death and *rigor mortis* was present. The body was somewhat emaciated. Neither the brain nor the spinal cord showed any change to the naked eye. The region of the thymus gland was occupied by fatty tissue. The thyroid weighed 20·5 grammes and was of natural consistence and appearance. Pancreas weighed 2 ozs. and seemed normal. Spleen was firm, and weighed $8\frac{1}{2}$ ozs. Kidneys were healthy except for a small yellow nodule in one pyramid, the size of a pin's head. Adrenals presented a few small fibrous nodules but were otherwise normal. The liver weighed 2 lbs. 9 ozs. and seemed healthy. The heart was natural except for a small yellow atheromatous patch on the ventricular flap of the mitral valve. The lungs contained air throughout, except the base of the left lower lobe which was plum-coloured and sank in water. The right ovary was cystic. The muscles had a healthy appearance.

Microscopical.

Central nervous system.—The Nissl and logwood-eosin methods were used for the examination of the motor cortex, the oculo-motor, facial and hypoglossal nuclei and the ganglion cells of the cord. The large majority of cells in all these regions were of a perfectly healthy type, and if a few were slightly swollen and pale there was certainly nothing like a true chromatolysis or atrophy to be seen. Weigert-Pal specimens of the motor cortex, the brain-stem and spinal cord were remarkable only for their normal appearance. Sections stained by Busch's method from the same regions must also be passed as normal, although a few isolated black dots were scattered about in the white matter. No lymphorrhages were seen in the brain or spinal cord.

Peripheral nerves.—Sections stained by the Weigert-Pal and Busch methods were made from the trigeminal, sciatic and ulnar nerves, but these presented no evidence of

pathological change. Other sections stained by the logwood-eosin method showed no obvious abnormality.

External ocular muscles.—The appearances presented by sections of these muscles were practically identical with those found in Case 1. Lymphorrhages were unusually small but fairly numerous and were unassociated with any other changes either in the muscular, nervous, or connective tissue elements.

Skeletal muscles.—Portions of many of these muscles were examined, but only in a few were lymphorrhages observed. Excellent examples, however, were obtained in the rectus abdominis, and one of these in longitudinal section is represented in Plate II., fig. 1. This one measures about ·7 mm. in length and ·25 mm. in its greatest breadth. An empty capillary, represented by its endothelial lining, was seen to traverse the centre of the mass of lymphocytes and the neighbouring fibres appeared to be perfectly healthy.

Apart from the presence of lymphorrhages only a few sections showed any other pathological conditions and these were much the same as have been described in Cases 1 and 2, but perhaps in a few instances of greater intensity. Rounded, swollen fibres with hyaline and homogeneous sarcoplasm were present, but in some the change had gone a step further, and alterations in the refractive properties of the central portions of the fibre, with pericentral vacuolation, or central nucleation and vacuolation, were occasionally observed and reminded one of the earliest stages of certain forms of muscular atrophy. With these exceptions, and they were comparatively rare, the muscles presented a very healthy appearance.

Cardiac muscle.—Attention must be drawn to the condition seen in Plate II., fig. 2, which pictures a capillary vessel crowded with white blood corpuscles, chiefly of the lymphocytic variety and unaccompanied by any red corpuscles. Some of these cells had escaped into the neighbouring tissues, but the specimen is unique in my series, and important in that it suggests the condition which precedes the production of a lymphorrhage.

No changes were observed in the heart muscle fibres themselves.

Liver.—The changes found in this organ were rather difficult to describe. Scattered here and there in the midst of healthy hepatic tissue were small areas from which the liver cells had disappeared and were replaced by necrotic *débris*, together with a number of small round cells, some of which had the appearance of lymphocytes and others had irregularly-shaped nuclei.

Dilated spaces containing a few cellular elements were occasionally seen in the substance of Glisson's capsule. As far as size, distribution and general appearances are concerned they were compatible with what may be supposed to be the ultimate remains of lymphorrhages, and the presence of the small cells, some of which may also be undergoing degenerative changes, lends some support to this view. At the same time I think it wiser to abstain from expressing any decided view as to their origin.

The greater part of the liver tissue appeared to be healthy, both microscopically and macroscopically.

Adrenal bodies.—In the case of these organs there could be no doubt as to the presence of lymphorrhages, which were numerous and in some cases of considerable size. They occurred in most instances in the inner or central parts of the cortex, although the medullary region was not spared entirely. Beyond the mechanical destruction of the glandular cells in the immediate neighbourhood, the adrenal tissue did not appear to be affected by their presence and would pass muster as healthy.

The spleen, pancreas and kidneys.—These viscera presented no pathological changes on microscopial examination.

The thyroid gland.—Dr. Chalmers Watson who kindly examined the slides prepared from this gland reports that there were: (1) Distinct interstitial fibrosis; (2) numerous areas of cellular infiltration resembling small abscesses (lymphorrhages); (3) a large area of colloid degeneration of the fibrous stroma in one part; (4) proliferation of the epithelium with formation of new vesicles in some regions; and (5) enlargement of spaces as seen in simple goitre.

Thymus gland.—Dr. Dudgeon reports that only islets of gland tissues could be seen scattered throughout dense connective and adipose tissue. In some places the adipose tissue was surrounded by glandular structure. The cortex could not be distinguished from the medulla and some endothelial proliferation was present. The concentric corpuscles were mostly in good condition, but some had undergone both granular and calcareous degeneration. No eosinophile cells were seen.

Case 4.—H. B., a schoolmaster, aged 40, was admitted to the National Hospital in October, 1899, under the care of Dr. T. Buzzard, and the following account is reproduced from the *British Medical Journal* of March 3, 1900, in which the clinical features of this case, along with another, were published.

Family history.—The patient's mother died of phthisis. His father, who is alive, aged 63, has suffered from muscular rheumatism. The grandparents on both sides are long-lived. The patient had four brothers and sisters, of whom a brother three years younger than himself is alive and strong; a sister died of scarlatina, two died in infancy. He has three children, aged 14, 10 and 8, all of whom are fairly strong, and there have been no deaths, no miscarriages. No similar condition to the patient's is known to exist among his relations. There is a rheumatic tendency in his father's family. A paternal uncle died in a lunatic asylum; a paternal aunt, aged 60, of "creeping paralysis."

Personal history. — Although never robust he was quite healthy till 1892. Twenty-eight years ago he had scarlatina, otherwise he has never had a day's illness until the present trouble. Syphilis can with certainty be excluded. There is no history of injury. He has not had a distinct attack of influenza. He is a total abstainer from alcohol, and not a heavy smoker. His work as a schoolmaster is hard and involves much speaking. His recreations have been chiefly of a sedentary nature, although he is fond of walking. He has had considerable worry during the last year or two.

Present illness.—Until 1892 he enjoyed good health. He then began to take a cold bath every morning, and is disposed to attribute his illness to this. About Christmas, 1892, after sawing wood, his little and ring fingers felt weak, but speedily recovered. The weakness recurred after playing the organ, and his right index finger would occasionally drop. In 1893 he occasionally

saw double, and this trouble recurred in 1894. About this time his voice, after speaking a few minutes, would acquire a nasal character. His right eyelid, too, tended to droop. This weakness in fingers and eyelids occasionally recurred, but not in a very marked form, during the three following years. In the summer of 1897 he felt weakness in the lips and tongue, and spoke through his nose. After speaking some time the voice would become feeble. He again saw double. In the vacation he walked eight or ten miles a day without fatigue for several days. After this his right thigh became weak. He found that he had frequently to stop and rest it for a few minutes, after which he could go on walking. He had never noticed this difficulty before. In the winter of 1897-98 both arms and hands were easily fatigued, and the right leg felt weak. In July, 1898, his speech was again affected, especially in the evenings. He walked sixteen miles in one day during the vacation, and although he found difficulty in accomplishing the last few miles, this was due rather to trouble with his breathing than with his legs. At times he would suffer from palpitation, which was new to him. In October, 1898, whilst suffering from catarrh, he had difficulty in coughing and clearing his throat, and also in swallowing. This cold seems to have pulled him down very much, and he has never recovered the strength which he had before. In January, 1899, his right arm was so weak that he could not brush his hair or write upon the blackboard, but after two days' rest he was able to move the arm quite well. At this time there was dull, aching pain in the right arm and leg, especially after exertion, but also sometimes whilst lying still in bed. At Easter, 1899, he again had ptosis of the right lid, which has persisted in varying degree since. In June he gave up work. Diplopia and masticatory difficulty were then his chief troubles, but from time to time he would also suffer from dyspnœa, especially after exertion or emotion. From August he again improved, but was subject to recurrences of all his troubles, especially in very hot or cold weather. After a considerable rest his symptoms almost entirely disappeared.

Condition on admission (October, 1899).—His face is somewhat expressionless, and there is right-sided ptosis. Intelligence is not impaired. After speaking a little his speech becomes slower, laboured, and indistinct, and the voice is nasal in character and gradually fails. He describes the lips and tongue as feeling tired. It is noticeable that the chest expands less and less with each succeeding breath. The change in speech would appear to depend

upon weakness of the respiratory muscles as well as those of articulation. Diplopia is only present on extreme lateral deviation to the right, and then only if the eyes are maintained for some considerable time in this position. The optic discs are normal. Hearing, taste, smell, and the viscera are unaffected. The ptosis is more marked in the evening, and is present to a slight extent also in the left eyelid; it is not always present. Two days after admission, when examined in the morning before rising, instead of ptosis there was actually retraction of the upper lids, so that a portion of the sclerotic was exposed above the cornea. Directly this condition was remarked upon the lid began to droop, illustrating what he says is one of the most characteristic features of his complaint, namely, that when his attention is drawn to any particular symptom, it will become exaggerated. He cannot voluntarily open his eyes widely, but when interested in conversation the lid moves upwards to a greater extent than he is capable of producing by any act of the will.

Ophthalmological examination.—Mr. Gunn, during his examination, remarked this incident, and attributed it to the action of Müller's muscle. Not only is he unable to open his eyes widely, but if he looks steadily upwards at an object held above his line of vision, the upper lids gradually droop lower and lower until the eyes are almost closed. Mr. Gunn reports: "Downward movement and convergence are good; upward movement defective; both external recti are weak. The pupils are equal, of moderate size, and react perfectly to light and on convergence; they dilate upon appealing to the patient's emotions, and occasionally upon mental concentration after prolonged convergence they show a great tendency to oscillatory movements."

Laryngological examination.—Sir Felix Semon, who was so good as to examine the palate and larynx, reports as follows: "The condition of the motor movements of the palate corresponds to what has been observed in the other voluntary muscles upon voluntary exertion. At first the palate is fairly well and symmetrically raised on phonating the letter A; gradually, however, as he repeats phonating, the movements become less and less marked, and finally hardly any raising of the palate is observed.

"On laryngoscopic examination, at first the larynx appears perfectly normal, except perhaps that on deep inspiration the vocal cords do not separate quite as much as in the ordinary condition; but as the patient, previous to the commencement of the examination, complained spontaneously of the shortness

of breath, this might have been due to his general inability to take a long breath. Closure of the glottis on phonation was, and remained, perfect; on repeating his endeavours at breathing deeply, the glottis certainly finally opened less than at first. It is very probable, however, that this phenomenon was only part and parcel of the general exhaustion."

Muscular System.—He is quite unable to raise the eyebrows and wrinkle the forehead, and can only frown slightly. He can close his eyes, but cannot screw them up firmly. He can whistle and show his teeth, but movement of the upper lip is feeble. Contraction of masseters, temporals and pterygoids is feeble. He says that the jaw will frequently drop, the muscles apparently being unable to support it. The masticatory muscles become tired in the act of eating. The lips feel weak after talking, and at night saliva will dribble from his mouth. Occasionally he feels twitching sensations about the face, though no movements have been noticed, but he is awakened sometimes by a champing movement of the lower jaw. There is at present no difficulty in swallowing. The tongue is protruded straight, promptly, and to its full extent. It is symmetrical, and the movements are good, but easily exhausted.

The muscular power of this patient is subject to great diurnal variations. Towards evening he often sits with his hands clasped behind his neck supporting his head, as though the neck were weak. There is a tendency for the head to fall backwards. He cannot sit up for very long without feeling the back weak. He cannot sit up in bed without using his hands. He has some difficulty in turning in bed.

The rapidity with which the respiratory muscles are fatigued is demonstrated when he reads. Respiration is abdominal in type. During respiration there is almost no thoracic expansion, the difference in circumference of the chest between extreme voluntary inspiration and expiration amounting to less than half an inch. No weakness of the diaphragm can be detected.

The movements of the upper extremities are feeble, the right more so than the left; the dynamometer grasp, right 45, left 50 (average man 160). The ready way in which the muscles of the hand become fatigued is demonstrated by asking him to button and unbutton his waistcoat repeatedly. As regards his writing, he begins to write rapidly, forming his letters well. After a few lines the writing becomes slower and laboured, and the letters are not so well formed. Finally he comes to a stop, more or less suddenly, unable to write further. After a minute or two's rest he is able to write again as well as at first.

He can raise his arms above his head, but cannot maintain them in this position for more than half a minute. They gradually fall; he feels as if heavy weights were attached to them. Again, after a short rest he performs the movement quite well. If requested to lift his arms quickly above his head several times in succession he will do this, but at each effort the arms are lifted less high, and after doing this seven or eight times they cannot be lifted at all, but hang by his sides. After a rest of from thirty to sixty seconds they can be lifted nearly as high as they were at first. All movements of the lower extremities are well and powerfully performed, but the right leg especially is easily fatigued. There is no muscular atrophy, nor are there any fibrillary twitchings. The muscles respond fairly well to direct stimulation with a percussion hammer and no diminution in the activity of the response results from repeated blows.

Sensation.—A dull aching in the neck, back, arms, and right leg, occurring particularly after exertion, but also when lying in bed, is sometimes present. No disturbances of cutaneous sensibility can be ascertained.

Reflexes.—The arm-jerks are present, feeble. The knee-jerks are present and equal, usually a little more active than the average. The patella-jerk is not depressed. Repeated attempts were made to determine whether the knee-jerk diminished after frequent tapping. On one occasion the tendon was tapped continuously for a quarter of an hour, but at the end of that time quite as good a knee-jerk was obtained as at first. No ankle clonus is present. No abdominal reflex was obtained. The plantar reflex is present, with sluggish flexor response.

Sphincters.—The bowels are regular. There is no trouble in commencing micturition, and the stream is well maintained.

Cranium and spinal column.—There is no abnormality. The gait is natural. After walking several times up and down the ward nothing abnormal is noticed. No vasomotor or trophic changes have been discovered.

Of great importance and interest are the results obtained by electrical examination. The muscles respond to faradism in varying degree on different occasions. For instance, if an electrode be placed upon the motor point of the biceps a prompt and good contraction is obtained, except when the muscle has been fatigued by voluntary exertion. The initial contraction in certain muscles is very much poorer than in others, and some muscles tire very much more easily than others. As the result of faradic stimulation, voluntary power of contracting the muscle stimulated

is much diminished and a feeling of fatigue induced. As regards galvanism, after repeated stimulation the muscular contractions become less, but the muscle cannot be tired to the same extent as is the case with the faradic current. No polar change can be demonstrated.

This patient left the hospital in the early part of 1900, but remained more or less in the same condition for the next few years. During the year 1903 he was hardly able to walk from one room to another, and always went out in a bath-chair. Every few weeks he would suffer from severe paroxysms of dyspnœa, and he ultimately died of respiratory failure on January 24, 1904. Owing to the kindness of Dr. Morrow, of Enfield, I was able to perform an autopsy twenty-two hours after death at the patient's house.

The body was extremely emaciated, but the muscles, though poor in size, preserved their natural contour and presented no evidence of local atrophy.

The brain and spinal cord with their meninges and vessels appeared normal to the naked eye. Portions of only a few of the larger muscles and nerves were removed for the examination, and unfortunately the ocular muscles were not among this number.

The heart, lungs, spleen, liver and kidneys showed no signs of disease. The pancreas had undergone *post-mortem* digestion.

The stomach and intestines were normal, and one or two spleniculi were found attached to the mesentery.

The thyroid was natural in size and appearance.

The thymus gland was rather unusually well developed, weighing 9·5 grammes after the adjacent fatty tissue had been stripped off.

Microscopical Nervous System.

The cells of the motor cortex were in excellent condition, and the same remark applies to those of the bulbar nuclei. A few small recent hæmorrhages were seen in the floor of the fourth ventricle. A careful examination of the cells of the cord was made, and it was thought that they appeared smaller than the normal on the average, but the difference was slight if present, and in other respects they lacked none of the healthy characteristics. A few capillary hæmorrhages

were noted in the gray matter of the anterior horns, but these were quite recent and associated with considerable congestion of the vessels.

The Weigert-Pal and Busch methods showed no alteration in myelinated fibres either in the central or peripheral nervous system, and sections of the cord and sciatic and ulnar nerves stained by logwood and eosin showed no pathological conditions.

Muscular system.—Owing to the circumstances under which the *post-mortem* examination was made only a few small pieces of muscle were investigated microscopically, and these came from the erectores spinæ, the left pronator radii teres and the left biceps femoris. In the sections examined, only one or two small lymphorrhages were found and the fibres as a whole were of healthy size and appearance. A certain number, however, were present in which a rounded swollen contour and homogeneous sarcoplasm were noted. No changes were detected in the vessels, connective tissue, or muscle spindles.

Spleen.—There was no thickening of sheath or septa and the relation of the pulp to the fibrous constituents was about normal. Malpighian bodies plentiful and well marked. A spleniculus was also cut and the sections presented similar appearances.

Pancreas.—This organ had undergone so much digestion that it was of no use from an histological point of view. In the loose areolar tissue surrounding the pancreas masses of lymphoid tissue were seen under the microscope having an appearance similar to the islets of thymus remains, but containing no Hassall's bodies. Some of the vessels in this tissue were closely surrounded by clusters of lymphocytes, and some had their lumina blocked with the same kind of cells.

Adrenals.—Numerous small lymphorrhages were seen in the sections of otherwise healthy glands. One of these is depicted in Plate I., fig. 2.

Thymus.—Report by Dr. Dudgeon. The gland is large and the cellular constituents are in good condition. The cortex and medulla can be differentiated from each other,

although the distinction is not so well marked as in the case of the normal organ. There is some increase in the fibrous stroma, and adipose tissue has replaced the glandular tissue in several parts. Many of the concentric corpuscles are very large and calcified, while others give evidence of granular degeneration. No eosinophiles are to be seen.

Case 5.—A man, aged 40, was admitted to the London Hospital, under the care of Dr. C. Wall, on February 10, 1905, with the history of a month's illness.

He was a foreman for a mineral water company. His wife was healthy and had had three children and two miscarriages.

He had suffered from "malaria" fourteen years previously, and since that time was subject to incontinence of fæces after taking aperient medicine.

Present illness.—One month ago he noticed such weakness of his neck that he could not hold his head up straight. The eyelids tended to droop, and he was unable to lift his arms above his head. Difficulty with articulation, mastication and deglutition was also observed, as well as considerable trouble in keeping food from collecting between his teeth and cheeks. Articulation would become worse after he had talked for a while, and diplopia was present at times.

Condition on admission.—The heart, lungs, and abdominal viscera appeared healthy on examination.

The optic discs were healthy. There was partial ptosis of both upper eyelids, weakness of the left external rectus and right internal rectus muscles. There was no nystagmus.

He was unable to protrude the tongue beyond the teeth, but no tremor was observed. All the muscles of the neck were paretic and he was incapable of raising his arms above his head.

Romberg's sign was absent. The knee-jerks were present and equal, and the plantars flexor in type.

February 22, 1905.—Patient had an attack of dyspnœa last night, and a bad fit of choking to-day while eating pudding. He can talk but little without becoming exhausted.

Electrical reactions. The myasthenic reaction is present in the trapezius of both sides, in the pectoralis major, the biceps and flexors of wrist on the right side. The triceps and deltoid muscles did not give the reaction, but it was present in the facial muscles, especially on the left side.

February 23.—Diplopia is marked, but the pupils react normally. The left upper eyelid droops more than the right.

The movements of the right eye are good, but there is complete paralysis of the left external rectus.

February 25.—Swallowing is best in the early morning, and becomes more difficult as the day goes on. He has had two more bad choking fits.

February 27.—There is marked improvement in the ptosis, swallowing and dyspnœa, and the double vision is less than it has been for weeks.

The patient's condition varied from day to day until April 6, when he had increasing difficulty in breathing, and was unable to cough up the mucus from his bronchial tubes. On the 7th his respiratory muscles became progressively weaker, and death took place from respiratory failure.

The autopsy I was kindly allowed to make at the London Hospital fifteen hours after death. The body had been frozen and *rigor mortis* was marked. No evidence of local atrophy or general emaciation was found on inspection.

The brain and spinal cord with their coverings appeared healthy to the naked eye. The pituitary body was normal. Portions of several peripheral nerves and of many muscles were kept for microscopical examination, but to the naked eye presented a natural appearance.

Thorax.—Behind the manubrium lay a large mass which on removal weighed 59·4 grammes. The upper part of this mass was firm and adherent to the subjacent vessels, the lower part was not so adherent and was softer and cystic. On cutting into the upper part it was found to be soft and creamy in the centre, and slide smears were prepared of the pus-like material. Closer examination of the lower portion showed that it was a thin-walled multilocular cyst containing a slightly cloudy fluid.

The lungs were healthy except for an old scar at the left apex.

The heart weighed 10 ounces and was free from any evidence of disease.

There were no enlarged bronchial or tracheal glands. The thyroid weighed 13 grammes and was pale in colour, but otherwise natural.

Abdomen.—The liver looked healthy and weighed 3½ lbs.

The spleen weighed 9½ ounces, was firm and showed prominent malpighian bodies.

The kidneys, pancreas, adrenals, stomach, and intestines, were all examined with negative results. The mesenteric glands and Peyer's patches were prominent without being unduly enlarged. A portion of the left femur was removed with the intention of examining the marrow, but it may be stated at once that this proved of negative value owing to the fatty, non-cellular condition of the latter.

Microscopical.

Owing to the acute course of the disease in this patient —the whole illness only lasted about three months—it was thought that the examination of the cells of the central nervous system would be of particular interest, and a number of sections, stained by Nissl's method, were prepared from the motor cortex, the oculomotor and bulbar regions, and from various levels of the spinal cord. After a careful investigation of these it was impossible to state that any definite pathological changes were present, although a certain number of anterior horn cells were somewhat deficient in tigroid. On the other hand, the oculomotor nuclei would pass as typical examples of healthy cells possessing abundant tigroid and central nucleation.

Serial sections of a cervical posterior root ganglion were stained by the same method and presented an entirely normal appearance.

As in the preceding cases neither the Weigert-Pal nor the Busch methods were successful in revealing any morbid condition in the central nervous system or in the peripheral nerves. Several of the latter were teased, but no abnormal fibres were seen.

Muscular system.—The ocular muscles contained several small and one or two larger lymphorrhages which differed in no particular from those seen in other cases.

The skeletal muscles, from a number of which sections were cut and stained, presented some features peculiar to this case and deserving of special mention.

Lymphorrhages of the usual type and of varying size

were found in a small proportion of the sections examined and were not always confined to the muscle fibres, as in one or two instances they occurred in the fibrous sheath of the muscle. In addition to the ordinary lymphorrhages a condition was found in a number of serial sections taken from a portion of the triceps muscle which is represented in Plate I., fig. 3. A cellular condition is associated in this instance with marked changes, in the form of swelling and protoplasmic disintegration, in the neighbouring muscle fibres. This reaction to the cellular exudation is unique among my specimens and is rendered more interesting by the fact that an examination of the cellular elements of the exudation showed that they differed from the cells usually seen in lymphorrhages. Some of the cells were probably true polymorphonuclear leucocytes but the nature of many of the others could not be definitely ascertained. Their size was very much that of lymphocytes, although some were larger, but they presented more clear protoplasm and contained nuclei which in many instances appeared to be undergoing division into two or four parts. Owing to the fact that they lay thickly together in celloidin sections accurate examination of their characters was impossible, and these facts can only be recorded without any attempt being made to define their true significance. It will be noticed that some of the altered muscle fibres were actually invaded by the cells, a condition which does not apparently obtain in the ordinary type of lymphorrhage.

In the neighbourhood of a small lymphorrhage, in another section, some of the fibres presented an appearance which is occasionally seen in conditions of very early muscular atrophy of toxic origin. In transverse section the fibre is rounded and in the centre is a dark core surrounded by a concentric ring of lighter hue; as far as can be ascertained the appearance is produced by an alteration in the refractive properties of the central and pericentric portions of the plasma, and not to the presence of nuclear elements on the one hand and of disintegration on the other.

In longitudinal sections evidence of early atrophy was also forthcoming here and there in the form of localised

swelling in a fibre and marked proliferation of the sarcolemma nuclei.

While attention is necessarily drawn to the morbid conditions discovered, it must be clearly understood that in this case, as in the others of my series, the large majority of fibres could not in any way be differentiated from those of healthy muscle.

Liver.—In otherwise normal sections a few well-marked lymphorrhages were seen, generally situated round and about the biliary ducts or blood-vessels.

Adrenals.—Microscopical preparations of these organs contained only one or two doubtful lymphorrhages of minute size, and the only feature of note was the intense congestion of all the blood-vessels associated with pallor of the gland cell nuclei.

Pancreas.—The histological appearances of this organ were of a healthy character.

Thyroid.—No lymphorrhages were found and no other abnormal features noted.

Thymus.—The examination of this organ included the preparation of: (1) smears from the semi-fluid matter contained in the centre of the upper solid portion, and from the liquid contained in the cystic portion of the gland; and (2) sections of the upper portion and of the multilocular cysts. These were stained by logwood and eosin, by Jenner's stain and by Leishman's stain.

The more solid part of the organ consisted of closely packed masses of ordinary thymus gland cells separated by dense bands of connective tissue; it contained no traces of Hassall's bodies. In the smears taken from this part the prevailing cell was of the lymphatic type, but there were also a considerable number of eosinophile cells of large size. The cystic portion resembled the solid part except for the fact that the dense masses of cells were replaced by a thin fluid containing similar cells in much smaller numbers. Owing to the pressure of this fluid the cyst walls appeared to have a definite lining membrane, but this was not of true cellular structure. In the midst of the fibrous strands composing the cyst walls many lymphocytic cells were entangled,

sometimes in large clumps, and a fair number of eosinophile cells were also observed. One or two doubtful remnants of concentric corpuscles were noted.

Pituitary body.—Sections showed no abnormality beyond some slight colloid degeneration in the glandular part of the body.

Clinical Summary.

The five cases here recorded, although varying very considerably in their duration, all presented the typical motor phenomena which we associate with myasthenia gravis, and each one exhibited the bulbar symptoms which at one time gave the name "asthenic bulbar palsy" to the disease. The disorders of motion are now so well known that it is unnecessary to dwell upon them here, and attention will be at once directed to certain other disorders presented by some of my cases which are more rare and less well recognised.

Sensory Phenomena.

In that excellent monograph on myasthenia published by Campbell and Bramwell (3) in 1900, the sensory side of the disease is dismissed in the few words "there are no sensory symptoms." In the five years which have elapsed since those words were written, a large number of cases of myasthenia have been recognised, carefully investigated and recorded, with the result that that statement no longer holds good. Subjective pains and paræsthesiæ of various kinds have been mentioned in connection with a number of cases, but as far as I am aware no case of the disease has presented such startling disorders of cutaneous sensibility as were found in Case 1 of this series. A reference to the charts will show that the relative analgesia and anæsthesia in this patient was progressively distributed over those areas of skin which nearly always show the same changes in cases of tabes dorsalis. When the reader remembers that these changes were associated in this patient with "lightning" pains, with absent arm-jerks, and with diminished knee-jerks, he will not be surprised to learn that the

possibility and even the probability of myasthenia being combined with early tabes was entertained during life.

The negative results obtained in a careful search for microscopical evidence of the latter disease, allow us to draw one of two alternative conclusions. The sensory disturbances are occasional, if rare, symptoms of the morbid process which we designate by the name "myasthenia," or the patient had a "functional tabes," by which is meant the disease in that early stage where the disorder of function precedes the anatomical lesion, if such a stage actually exists.

The second of these two alternative propositions is one which it is impossible to support with any material evidence at the present time, but the first may be considered in the light of contrast with other cases. Case 2 complained of intermittent sharp pains similar in character to those described by Case 1, and had in addition a small patch of relative analgesia and anæsthesia during a period of the time she was under observation. Senator (7) describes a case in which there was anæsthesia of the chin, and Burr (2) has mentioned the presence of some very interesting visual disturbances in one of the cases which he has reported. It can hardly be denied, therefore, that sensory phenomena may take a prominent place in the symptomatology of the disease, and their presence can no longer be held to be sufficient to throw doubt upon the diagnosis.

The explanation of their occurrence is a most difficult problem, but hardly more so than that of the motor phenomena. Some reference to this subject will be made in discussing the question of pathogenesis.

In this connection it may be interesting to mention that an undoubted case of myasthenia which was under my observation for two or three years, presented unmistakable evidence of mental changes which varied in intensity from time to time. Melancholia with delusions of persecution and some suicidal tendencies were very marked for short periods, and I have in my possession letters from the patient which illustrate well the morbid condition of his mind. Unfortunately I was unable to obtain an autopsy at his

death. This experience again makes one hesitate to accept the dictum of Hun (4) that "mental abnormalities play no part in this disease."

Muscular Atrophy.

The occurrence of localised muscular wasting in myasthenia has been doubted, but recent records favour the view that it is certainly present in some cases. The tongue is a favourite site for atrophic change, and in Dr. Head's case there was definite wasting of the temporal muscles. Although I have never had the opportunity of examining histologically any markedly wasted muscle in this disease, I am satisfied from clinical observations that such wasting does occur in some instances.

Morbid Anatomy.

In studying the records of cases of myasthenia which have been examined after death, it is found that in a large number the results have been negative, or variable and trifling, but that in a smaller number, and these belong to recent years, attention has been drawn to the existence of changes in the thymus gland and to the presence of lymphocytic deposits in the muscles. A considerable variety of thymus changes have been described, including so-called thymus tumours (possibly lymphosarcomata) and different degrees of thymus enlargement, and the view has been held that the lymphoid tissue found in the muscles has been of the nature of metastases. My cases show that abnormalities of the thymus are *not constant* features in this disease, and therefore that the lymphocytic deposits, which occur independently of them, are probably not in any way a secondary condition. On the other hand my experience affords reasonable grounds for believing that lymphorrhages are constantly present in the muscles or other organs in cases of myasthenia. That they existed in all five of my cases was only established by a diligent search through some thousands of sections, and for that reason it would be unwise to assume that they were absent from the cases of other observers who had not been led to conduct a similar

careful investigation with the same object. Moreover, it is interesting to note that since their presence was first described their occurrence has been reported in an increasing number of cases. I would suggest that this number will be still greater when it is realised that a persistent thymus or a mediastinal tumour is not a necessary concomitant of the lymphorrhages. An exhaustive examination of all the muscles is too laborious a task for any investigator to undertake, but it is fairly easy thoroughly to search the ocular muscles and a number of selected samples from various skeletal muscles. The presence of lymphorrhages in other organs, described here for the first time, renders the undertaking still less formidable.

Although the occurrence of a thymus gland of unusual size or with pathological features is not, as we have seen, a constant factor, yet its frequency is so considerable that it will be impossible to disregard it in discussing the pathogenesis of the disease.

Out of my five cases one presented a very large thymus gland which had undergone changes partly proliferative and partly degenerative in nature, another exhibited considerable simple hypertrophy of the gland, a third a minor degree of the same change, while in the two remaining patients were found only those islets of lymphoid tissue which are commonly present in the adult human being.

Lymphorrhages were present in varying numbers in all five cases, but were by no means confined to the muscles. In several cases they were seen in the heart, liver, adrenals and thyroid gland. A considerable increase of round cells in parts of the kidney of at least one case was evident, but it was difficult to say whether the condition was identical with the lymphorrhages of other organs. In one instance (Case 1) there were scattered small foci of lymphocytes around vessels in the substance of several posterior root ganglia, and these I believe, after some hesitation, to be small lymphorrhages.

What is the origin and what is the fate of a lymphorrhage? To these questions I find it impossible to give a definite answer. The impressions gained from examining

a large number of these cell deposits inclines one to the view that they arise in some way from the capillary blood-vessels, and this feeling is strengthened by the fact that no evidence of any lymphatic disease has been forthcoming. At the same time we are shaken in our belief by the absence of blood changes during life and by the knowledge that the lymphocytes are not the most migratory of blood cells.

Certain appearances which would seem to give some support to the view that lymphorrhages are of vascular origin have been described in the preceding records of the cases but may be referred to again in this place.

In the first place the close association of the lymphocytic exudation with a small blood-vessel has been noted repeatedly. In Plate II., fig. 2, a capillary vessel is seen to be engorged at one point with white corpuscles, some of which have escaped into the surrounding tissues. In Case 2 attention has been directed to a cardiac blood-vessel full of red corpuscles, but surrounded by a mixed serous and lymphocytic exudation. A somewhat similar condition was seen in the liver sections of Case 3, in which dilated spaces containing amorphous *débris* and a few white cells were found in parts of Glisson's capsule. It would be premature to argue dogmatically from those preparations, but they certainly seem to throw some light upon the formation of these cellular deposits.

With regard to the fate of the lymphorrhages we can only suppose that they are transitory phenomena, since they are not more numerous, if as numerous, in long-standing cases as in those which run an acute and rapidly fatal course. Does the prevalence of lymphorrhages in a muscle bear any relation to the functional activity of that muscle? The data at my disposal are inadequate for the purpose of forming any opinion on this question.

The possibility that lymphorrhages might occur in other conditions was one which naturally arose, and an effort was made to settle the point by examining sections of muscles obtained from various other diseases of muscular or nervous origin. The ocular muscles from a case of pontine tumour, in which there had been ophthalmoplegia

for many months before death, were investigated with negative results. In a variety of other conditions the skeletal muscles were searched, but in only one instance was there found any appearances resembling the lymphorrhages described above. The case was one of amyotrophic lateral sclerosis which ran a very atypical clinical course, and in which the lymphocytic deposits were associated with extensive and unusual changes in the muscular fibres. In another example of the same disease no lymphorrhages were observed.

Although the lymphorrhages appear to be the most striking of the anatomical changes in myasthenia, yet it is desirable to point out that in every one of my cases some of the muscles have shown abnormal appearances in a small proportion of their fibres. These abnormalities have not always been identical, but they have all been of the character which one associates with an early stage of muscular atrophy, and suggest that they would have resulted in grave muscular degeneration had the morbid process at work been further encouraged. They certainly make the occasional occurrence of true muscular atrophy in this disease by no means surprising.

Attention having been directed to certain positive factors in the morbid anatomy it will be well to emphasise the untrustworthiness of certain negative factors. For instance, there can be little doubt that the methods at our disposal for the examination of the axis cylinders in nerve trunks, and more especially the terminations of neurofibrils in their muscular connections, are inadequate, and it is impossible, therefore, to feel certain that these important structures do not show definite, but hitherto undetected, alterations. At the same time we should expect that permanent structural changes in these tissues would lead to some recognisable reactions, either in the myelin sheaths, or in the neurone cells, and of such there is no evidence.

The discovery of small lymphoid masses resembling thymic islets, except for the absence of Hassall's corpuscles, in the peripancreatic connective tissue of Case 4, makes one regret that more of this tissue in various parts of the body was not examined.

Pathogenesis.

Great as has been the increase in our knowledge of myasthenia within recent years, it is undeniable that the pathogenesis of the disease is still far from clear, and it is not my intention to discuss the problems with which we are faced at any length. At the same time it may not be unprofitable to refer to some points which are suggested by the cases just described, as well as to some further points observed in other cases, and to review them in the light of recent theories on muscular and glandular physiology.

A few years ago, Dr. H. D. Singer and I carried out some investigations on two cases of myasthenia in the National Hospital, some results of which I will briefly summarise here.

(*a*) Biceps humeri. With faradic current, the muscle rapidly ceased to be tetanised, the subsequent contractions being intermittent for a time and then ceasing altogether. By this time voluntary power was much diminished but not lost, the biceps-jerk remained unchanged, the galvanic reaction was brisk, and direct excitability to percussion was as lively as before.

(*b*) Same muscle. The muscle was rapidly tired out by voluntary action. Diminished faradic excitability was then present. The galvanic reaction, the tendon-jerk and direct excitability were unaltered.

(*c*) Same muscle. Rapidly repeated galvanic shocks for two minutes produced no diminution in the briskness or size of the response.

(*d*) Same muscle. Faradism with moderate strength of current was continued until no response was obtained. An increase in the strength of current immediately produced a contraction which was rapidly exhausted.

(*e*) Same muscle. The tendon-jerk was not diminished by rapid repetition for a considerable time.

(*f*) Attempts were made to ascertain the effect of exhaustion of one group of muscles upon the activity of another but the results were variable. General clinical observations seem to show, however, that there is a general reduction of power produced by local exhaustion.

(*g*) The same muscle in another patient, very weak and quickly tired. Tendon-jerk absent. Direct excitability to percussion less than normal.

After exhaustion by faradism there was still further loss of voluntary power. After further exhaustion by voluntary action there was dimished reaction to faradism. Galvanic response good and brisk.

The muscle was exhausted by faradism and then by voluntary action. When it ceased to respond to volition it had regained some response to faradism; galvanic response still good.

The above observations, which were made at a number of different sittings, admit of course, of various interpretations, but they appear to me to suggest certain conclusions. In the first place the exhaustion of a myasthenic muscle is always a relative phenomenon, and bears a definite relation to the nature and probably to the strength of stimulus employed. In the second place the liability to exhaustion is much more pronounced in the case of tetanising stimuli, such as are employed in voluntary action and faradism, than in the case of stimuli producing single sharp contractions such as direct percussion, indirect excitation through the tendon and galvanism.

Thirdly, I would emphasise most strongly the fact that no comparison should be drawn between the phenomena observed in myasthenic muscles and those which we associate with the reaction of degeneration. In the former case a muscle which has lost its response to faradism gives the normal brisk response to the make and break of a galvanic current. In the latter case a muscle, irresponsive to induction currents, gives a slow worm-like contraction on applying or discontinuing the galvanic current.

Jotezko (5) has shown that the slow contraction just mentioned is an idiomuscular phenomenon, and this fact, taken in conjunction with those just mentioned, distinctly contravenes the theory that in myasthenia we have to deal with an exhaustion or liability to exhaustion on the part of the muscular nerve endings.

Botazzi (1) has advanced the view, which is supported by

Jotezko (6), that in muscle there are two contractile substances, a fibrillar and a protoplasmic. The fibrillar contraction is the short sharp response, such as is produced by the make or break of a galvanic current; the protoplasmic contraction is slow and resembles that which is seen in the reaction of degeneration. They can both be produced by the galvanic current, but the protoplasmic reaction requires a stronger stimulus than the fibrillar. After nerve section the muscle tends to return to an embryonic condition, in which the fibrillar substance diminishes and the sarcoplasm relatively increases. Assuming these views to be correct they would help to explain the paradoxical condition observed in the myasthenic reaction, and we might suggest that in the disease under consideration, some agent is at work which reduces the excitability of the protoplasmic more than that of the fibrillar constituents of the muscle.

Going a step further it may be asked, what evidence is there of the presence of a toxic agent of either exogenous or endogenous origin? So far as our knowledge goes there is no good reason for believing that any microbe is the causative agent of the disease; on the other hand the clinical features of myasthenia present many resemblances to those of what are called the internal secretion diseases and especially to Graves' disease and to Addison's disease. With that idea in my mind, the ductless and other glands have been the object of much attention in the histological examination of my cases, but the results have not been illuminating. It is true that several of the glands have been shown to be the site of lymphorrhages but these are so widespread in their occurrence in these cases that their presence can only be regarded as part of a general condition and not as the specific cause of morbid glandular function.

The frequent abnormalities in the thymus are interesting in this connection but their inconstancy is a bar to attaching too much importance to them. At the same time it is well to remember that experimental observations have led to the belief that the thymus has some excito-motor influence when injected into animals.

The fact that the thymus is mainly a lymphatic

structure and that lymphorrhages form a prominent feature of the morbid anatomy of the disease, will doubtless lead to further investigation of the lymphatic system in myasthenia, and in this direction lies our best hope of solving the problem of its pathogenesis.

I have stated above that I was unable to estimate the relation of lymphorrhages to the functional activity of a muscle, but on clinical and anatomical grounds it would seem quite likely that some such relation may exist. The probability that lymphorrhages are temporary phenomena and the fact that muscles are irregularly, variably and sometimes suddenly affected in the course of the disease, suggest that in addition to a general morbid process there may also be local factors influencing its incidence. While admitting this I do not feel inclined to support the view that lymphorrhages exert a deleterious influence on muscular activity by the mechanical effect of their presence or by blocking the local lymph flow. As I have said in a former paper I prefer to regard them as the outward and visible sign of some more subtle—metabolic or chemical—influence which is exerting itself upon the function and in extreme and rare instances, upon the actual structure of muscular and other tissues.

It is necessary to assume that the toxic agent is capable of exerting an influence on the function of other tissues besides muscle in order to account for the sensory, mental, vasomotor and secretory disorders occasionally met with in the disease, but it is impossible to say at the present time whether a disorder of any one of these functions is always associated with the anatomical presence of lymphorrhages in the tissues subserving that function. In this connection I can only point with diffidence to the occurrence of cellular exudations, resembling in their histological features lymphorrhages of other tissues, in the posterior root ganglia of Case 1, the only patient of my series in whom diminution of cutaneous sensibility of root distribution was observed during life.

As a result of my experience and in order to remedy the defects in my own investigation I would advocate more

attention being directed to the condition of the blood, the marrow, the lymphatic system, and last, but not least, to the fatty and connective tissues of the body in cases of this disease which come to *post-mortem* examination.

The conclusions to be drawn from this investigation may be briefly summarised thus :—

Clinical.

(1) That myasthenia gravis is a disease in which the symptoms are not always confined to the motor system, but may include others of sensory, mental or other origin.

Anatomical.

(2) That in all probability it has a definite and constant morbid anatomy constituted by the presence of widely distributed cellular, and sometimes serous, exudations (lymphorrhages) in the tissues and organs of the body.

(3) That slight muscle-fibre changes are frequent and severe muscular atrophy rare occurrences in the disease.

(4) That proliferative and degenerative changes in the thymus gland are frequently but not constantly met with.

Theoretical.

(5) That the symptoms of the disease are best explained by assuming the presence of some toxic, possibly autotoxic, agent which has a special influence on the protoplasmic constituent of voluntary muscle and a less specialised influence on the function of other tissues.

(6) That the relation of this toxin to the incidence of lymphorrhages and to thymic alterations is not clear.

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ATAXIA IN CHILDHOOD.

BY FREDERICK E. BATTEN, M.D.

Physician to the Hospital for Sick Children, Great Ormond Street, and Assistant Physician to the National Hospital.

Introduction.

Certain well-known forms of ataxia occurring in children are commonly recognised, such as the ataxia of Friedreich's disease, the ataxia which occurs in tumours and lesions of the cerebellum and mid-brain, and in certain cases of diphtheritic paralysis. It is not with these well-known forms of ataxia that the present paper deals, but with certain cases of ataxia occurring in children which cannot be placed into one of the above groups. The instances on which the present paper is based have been seen, for the most part, at the Children's Hospital, Great Ormond Street, during the past ten years, and my thanks are due to several of my colleagues for not only allowing me to see patients under their care, but also for permission to refer to the same.

These cases, which may be classified as cerebellar diplegia, divide themselves into three groups.

(1) Cases in which ataxia has been noted early in life, and in which there is a tendency to gradual improvement (congenital cerebellar ataxia).

(2) Cases in which ataxia has suddenly developed after some acute illness in a child who formerly had been quite healthy (acute ataxia, encephalitis cerebelli).

(3) Cases in which a child has been healthy till a certain age, and then has gradually developed ataxia; cases in some points resembling Friedreich's disease, but differing from the classical picture of that disease (progressive cerebellar ataxia).

Group I.—Congenital Cerebellar Ataxia.

The following may be taken as the leading features of the disease :—

A child, whose backwardness in development is evidenced by the late period at which it learns to sit up, to walk, and to talk, is noticed when a few months old to "tremble" when using its hands; to this little or no attention is usually paid, but when on sitting up it is noticed that the child shakes its head and the whole trunk is in constant oscillation, some defect is first recognised by the mother and advice is sought. Nystagmus of the eyes on attempting to fix an object may be present. When the child learns to stand, it is noticed that there is great unsteadiness of the legs, and on attempting to walk the legs are thrown about in a most ataxic manner. As the child learns to talk the words are pronounced in a slow, jerky, and monotonous manner. Many of these children are slow eaters, and, though they will swallow liquids well, swallow solids very slowly. They are clean in their habits, take an intelligent interest in all their surroundings, and are usually well nourished, and have good muscular power. As they grow, the ataxia of the arms and legs becomes less, their articulation improves, and in the slightest cases normal development takes place. The following cases may be taken as a fairly typical example of this group :—

Case 1.—D. S., aged 4, was first seen in February, 1899. She was the first and only child, and there had been no miscarriages. The labour had been prolonged, and instruments had been used to deliver the child. The mother was in good health during pregnancy. The child was brought to the hospital because she could not walk. She had not learnt to use her hands till she was 12 months old, and, though she could talk, her articulation was so defective that it was difficult to understand her. She had always had difficulty in swallowing, and had to be fed very slowly; the difficulty was greater with solids than with liquids. She was intelligent and clean in her habits, and had never had any illness.

On examination the child was well formed and nourished; she could stand and support her weight on the legs, but was unable

to walk, and always tended to fall backwards. When an attempt was made to walk, the legs were thrown about in a wildly ataxic manner. The head and trunk were in constant movement, and, on attempting to grasp an object with the hands, the most marked inco-ordination and intention tremor were exhibited. The head was well formed, measuring 19½ inches in circumference, and there was no deformity of the skull. The movements of the eyes were good in all directions, and there was no nystagmus. The optic discs were normal. The hearing was good, the tongue protruded normally, and the hard and soft palate were normal. The back was straight, and there was no bony deformity either of the limbs, feet, or hands. The power of movement of the limbs was good, and there was no rigidity. The knee-jerks were brisk and equal. There was no ankle clonus, and the plantar reflexes usually gave extension of the great toe.

In October, 1899, she was seen again, and on this occasion could walk with great difficulty, and showed the same tendency to fall backwards. In February, 1900, her walking had improved, but she still tended to fall backwards. The head measured 20 ins. in circumference. The knee-jerks were brisk, and the plantar reflexes were noted as giving an indefinite extensor response, *i.e.*, the big toe extended, the small toes flexed.

In May, 1900, her walking had greatly improved. She could walk by herself, but still tended to fall backwards. She had much less inco-ordination of the hands, but the articulation was still very defective.

In March, 1901, she walked fairly well, with the trunk held forward in a position resembling that of paralysis agitans. The inco-ordination of the limbs and trunk was still present, but was comparatively slight. The knee-jerks remained active, and the plantar reflexes gave varying responses, sometimes extensor, sometimes flexor. The child was six years old when last seen, and appeared to have good intellectual development.

Case 2.—H. T., aged 3 years and 3 months when first seen in June, 1902. He had learnt to talk when 2 years old, and was bright and intelligent, but he had never learnt to walk.

He was unsteady with his hands, and could only stand when his back was against the wall. He took food well and swallowed naturally. He was clean in his habits, but sometimes had an "accident," which greatly annoyed him. He was not passionate. He was the first of two children, and there had been no miscarriages. The mother stated that she was not in good health during pregnancy, but the labour was natural and rapid.

The child was a well-nourished, intelligent little boy, with the slow, monotonous articulation characteristic of this affection; but he had in addition a lisp, so that he omitted the first consonant of a word: for example, he said "oor" for door.

He stood unsteadily, and seemed always likely to fall. He walked with the knees flexed and close together, like a patient with cerebral diplegia of a mild type, but at the same time there was marked inco-ordination. The legs could not be said to be rigid, although the mother stated that they were so at times.

The knee-jerks were present, not very active; there was no ankle clonus, and the plantars gave a flexor response, though it was a response which was neither easy to obtain nor definite in character. All the movements of the face were good, the movements of the eyes were good, the pupils were equal and reacted well to light; there was no nystagmus. The child sat up fairly well, but there was almost constant irregular movement of the trunk.

There was no curvature of the spine. There was no rigidity of the arms; the grasp was good, but there was marked inco-ordination of both hands on attempting to pick up a penny; the intention tremor was, however, slight. The child was seen again in December, 1902. He had learnt to walk, but the gait was still ataxic. He could sit up, but could not balance himself in a chair without sides. The knee-jerks were brisk; there was no ankle clonus, and the plantar reflexes were flexor in type.

In March, 1903, he had made further improvement, but was still somewhat ataxic. Knee-jerks were present.

In August, 1905, he was again seen. He was now 6 years old, and well grown. He attended an infants' school, and was stated to have normal intelligence. He was still unsteady in walking, but the movements resembled those of chorea rather than ataxia. He could walk quite safely across the room, and could get up from the floor in a normal manner. His mother stated that he could now go upstairs, whereas formerly he had been unable to do so. His articulation was fairly good, but still had a somewhat jerky character. The inco-ordination of the hands was slight. The knee-jerks were obtained; the plantar reflex was indefinite, but was generally flexor in character.

In a lecture published in the *Clinical Journal* (21), I have given a series of cases showing the gradual transition between the condition above described and that of a typical cerebral diplegia with rigid extension of the limbs.

In the discussion which follows I have suggested tha the experimental evidence derived from the ablation of the cerebellum throws considerable light on this subject, for it has been shown by Luciani (1) that animals rapidly recover from the symptoms produced by ablation of the cerebellum, if the cerebral cortex remains undamaged, but if the cerebral cortex be injured in the region of the gyrus sigmoidea, then the symptoms produced by the removal of the cerebellum persist.

This experiment would seem to explain the well-known clinical fact that there may be atrophy, and even complete absence of the cerebellum without any symptoms pointing to cerebellar disease being present. In the class of case under consideration, it would seem probable that there had been some damage to, or lack of development in the cerebellum and cerebrum at or before birth. As the cerebrum becomes developed, so it assumes the co-ordinating function of the cerebellum, and recovery more or less complete takes place according to the condition of the cerebral cortex.

One of the slightest cases which I have had the opportunity of observing was that of a boy, aged 2 years, who was seen in consultation with Dr. Sinclair, of Dundee. The boy began to walk at 18 months, and it was then noticed that he was very awkward in walking. On examination when 2 years old, although he could with accuracy kick a small ball with the right foot, he was unable to do so with the left, and his attempts to do so were markedly inco-ordinate.

Group II.—Acute Ataxia (Encephalitis Cerebelli).

Under the second heading, "acute ataxia," are arranged a series of cases which may be said to have the following characteristic symptoms.

A child perfectly healthy and of good intellectual development is taken ill with some acute febrile disease, which may assume some definite type, such as measles, or may be assigned to the more indefinite influenza. A period of unconsciousness may be present, but general convulsions seldom occur. The child is kept in bed for a few days and seems to be making a normal convalescence. When, how-

ever, the child is sat up in bed, it is found that he is unable to maintain his balance. There is marked inco-ordination of the hands, and, if stood on his feet, he is wildly ataxic. It may be noticed at the same time that his speech is affected. In a few days his general health is restored, but he remains as ataxic as ever. Recovery now gradually takes place, and although in a few cases recovery may be complete in two or three months, in most cases the period of recovery extends over several months, and it may be two or three years.

Such are the main features of the disease, and the following cases illustrate the type:—

Case 3.—G. S., aged 4½, was well till a slight attack of whooping cough in December, 1900. Towards the end of December, she had a disease described as influenza, for which she was medically attended. She was feverish for about a week, and vomited several times. She then developed paresis of the legs and affection of speech, and had also some slight affection of the sphincters. The child had but little headache, and never lost consciousness.

She was the eldest of three children—the other two had whooping cough. The child was first seen on February 7, 1901. She was a well-nourished, healthy-looking child. She could just stand with the legs wide apart, but was unable to walk and tended to fall straight backwards. The gait on attempting to walk was wildly ataxic. There was marked inco-ordination of the hands, the *right* being more ataxic than the left. The grasp of both hands was feeble and ill-sustained.

When laughing, the left side of the face moved better than the right. The ocular movements were good in all directions, except there was some defective upward movement of the right eye. There was no nystagmus, the pupils reacted well to light, and there was no optic neuritis. Articulation was somewhat bulbar in character, but there was no aphasia. The knee-jerks were equal and active; there was doubtful ankle clonus, and the plantars gave a doubtful response. The child was admitted to the hospital, made a rapid and complete recovery, and when seen some three months later was quite well. The plantar reflexes still gave a doubtful response.

It may be argued in this case that lesion was situated in the region of the mid-brain rather than in the cerebellum, as evidenced by the defect in the movements of the face in the

expression of emotion, and in the defective upward movements of the eye. The condition of the knee-jerk, the presence of ankle clonus and the plantar response might also be called in support of such a view, and with this view I should be in agreement, but the cerebellar symptoms are produced by involvement of the fibres of the superior cerebellar peduncles in their course toward the red nucleus; and the ataxia may well be considered of cerebellar origin.

Case 4.—A boy, aged 3½ years, developed measles in March, 1904, up to which time he had been perfectly healthy. During convalescence he had an attack in which he vomited, became unconscious and had a series of general convulsions. The stage of unconsciousness lasted for about one week. On April 9, 1904, he was quite conscious, but his arms and legs shook and he was unable to sit up, and could not speak.

The father of the boy is said to have phthisis, and one child in the family has died of tuberculosis.

The boy was first seen on May 13, 1904. He was well nourished and appeared intelligent. He spoke in a slow, hesitating manner. He was unable to sit up in bed without support, and when placed on his legs, walked in the most ataxic manner, flinging his legs about in all directions. There was marked incoordination of both hands, but the grasp was fairly good and equal on both sides. There was no facial weakness, no ocular paresis or nystagmus, and the optic discs were quite normal.

The knee-jerks were active, there was a slight tendency to ankle clonus on both sides, and the plantar reflexes generally gave flexor responses; but on one or two occasions a distinct extensor response was obtained.

Sensation was unimpaired, and all the superficial reflexes were normal.

The mother stated that since his illness the boy has been most untruthful. Not only did he tell lies to obtain his purpose, but he invented stories which could obtain him no possible advantage. His moral sense was perverted.

He was under treatment for some time in the hospital, but made but little progress, and when discharged in July, 1904, was still very ataxic.

He was seen again in November, 1904, and by that time had improved to a slight extent, but was still very ataxic in walking.

In June, 1905, he again came under observation, and considerable improvement had now taken place in his gait and also in the

co-ordination of the hands. His articulation was still defective. The knee-jerks were active, and the plantars gave flexor responses. He was seen again in October, 1905, and had improved in every way, and very little manifestation of his former ailment existed.

Another case was that of a child, who was shown by Dr. A. F. Voelcker before the Neurological Society in June, 1905 (*vide* p. 360 of the present volume).

Case 5.—A girl, aged $4\frac{3}{4}$ years, was supposed to have had an attack of scarlet fever at Christmas, 1904, during which she became unconscious for fourteen days; gradually she recovered consciousness, but has been unable to stand or feed herself since. Her speech was lost, but had gradually returned. There was no vomiting during the initial illness. When first seen, the child was unable to walk or stand, and could hardly sit up in bed. There was also constant tremor of the head. When supported, her gait was markedly ataxic, and at times the progression was cross-legged. There was a tendency to fall backwards. There was marked muscular hypotonus. The knee-jerks were brisk; there was no ankle clonus, and the plantar reflexes were variable, an extensor response being sometimes elicited on the left side. Only slight improvement took place during the two months the child was under observation. When seen in December, 1905, the child showed but little improvement, the plantar reflexes being still variable.

A similar case recorded by Dr. Leonard Guthrie was shown at the same meeting of the Neurological Society (*vide* p. 363).

A girl, aged 7 years, in February, 1904, at the height of an attack of measles, with a temperature of 103° to 104°, developed cerebral symptoms, vomiting, convulsions, unconsciousness followed by squint, retraction of the head, and photophobia. After five days all the acute symptoms subsided, but the patient was aphasic, seemed hyperæsthetic, and rapidly wasted. The optic discs were normal. A month later she was still aphasic, could not sit up or move lower limbs; the knee-jerks were exaggerated, ankle clonus was present, but no Babinski plantar reflex was obtained. There was marked inco-ordination of the upper limbs, and some athetoid movements of the fingers. There was general anæsthesia to pin pricks, but she recognised hot and cold, and appeared to fear pinching. All limbs were slightly rigid. Sphincter control was lost for two months. Then gradual improvement

occurred. By the end of May, 1904, she could stand with support, feed herself, and talk.

The child is described as healthy and well nourished. She was mentally slow, but not deficient. Her speech was drawling and bleating in character. Movements of the eyes were normal. There was slight ataxia and tremor of the upper extremities. She could stand alone and steadily when the eyes were closed, but could not walk more than a few steps without guidance. If left alone she reeled, turned half round, and fell backwards or to one side or the other. Loss of equilibrium seemed due to ataxy in placing the feet rather than to vertigo. The gait was ataxic. The knee-jerks were brisk, ankle clonus was present at times. Plantar response was negative or flexor.

The last case in this group which I shall describe is that recorded by Dr. Frederick Taylor (2), and it is of the greatest interest, since it proves that complete and absolute recovery may take place, so that in adult life the patient is able to undertake and perform the usual routine of life.

A boy, aged 4, was admitted to the Evelina Hospital on June 17, 1875. The boy had had whooping-cough three weeks previously. Eight weeks previously he had fallen down three stairs, but did not seem much hurt. For three weeks it had been noticed that his eyes twitched, and he dropped things out of his hand, and was unable to walk. He had vomited after food. He could not stand by himself, and when sitting up he was unsteady, bending slightly forward, and then recovering himself. He could pick up a pin with his fingers. There was occasionally lateral nystagmus. The chief characteristic of the case was the trembling of the limbs and trunk, which had a close resemblance to that of disseminated sclerosis, so much so that the late Dr. Moxon was asked to see the patient, but he believed that the symptoms were due to a cerebellar lesion.

The limbs were quiet as he lay passively in bed, and only trembled to any considerable extent when he sat up or lifted his arms to take hold of an object. Even then the movements were not violent; they were quick and short, but not extensive. The eyes were often examined with the ophthalmoscope, but no change in the fundus was ever seen. During the fortnight after his admission he was several times sick, but the vomiting ceased after June 30. During the next two months there was very little change. On leaving the hospital in September he was said to be

better than before. In the summer of 1876 he was said to have much improved in strength, though still suffering from trembling movements.

In February, 1877, he was again seen. He was fairly intelligent looking. On level ground he could get along in a highly ataxic manner. His movements were precisely those of a drunken man. He did not waddle or throw out his legs with the usual ataxia of tabes dorsalis, but having placed one foot on the ground, he could not balance himself sufficiently long on it to put the other in the right place—thus for a few steps he would plunge headlong forward, only just saving himself from a fall, then he would pull up and steady himself. Another moment and he was again staggering forward, frequently crossing one leg in front of the other.

He appeared to have good strength in his legs, for he was lively and active. He seemed in constant danger of falling, but seldom fell. The arms were ataxic. Tremor of the head and neck was scarcely noticeable. His sensation was apparently normal, and he was a lively, cheerful boy. His speech was hesitating and his voice was not properly modulated.

In November, 1878, he was said to have wonderfully improved. His speech was a little imperfect, but he was able to run and to bowl a hoop.

In November, 1904, he was seen again. He was 33 years of age and a clerk. No sign of his former complaint existed; he was an active man, and included hockey among his recreations.

Group III.—Progressive Cerebellar Ataxia.

Under the third heading, progressive cerebellar ataxia, are arranged a series of cases which may be said to have the following characteristic symptoms:—

A child who has been perfectly healthy and of normal development till a certain age, gradually develops ataxia, which slowly increases so as ultimately to render the patient incompetent to get about. These cases in some points resemble Friedreich's disease, in others Marie and Sanger Brown's hereditary ataxy, but differ from these diseases in many particulars, so that though undoubtedly allied to those conditions, find a place under the present article, not as a separate disease, but as a member of that great group cerebellar and spinal ataxia.

The following case which was under the care of Dr. Voelcker, who regarded it as a case of disseminated sclerosis, was shown at the Neurological Society, June, 1905, illustrates the main features of the disease, and the published cases of Fraser (3), Michell Clarke (4) and Warrington (5) complete the clinical picture.

Case 6.—M. C., aged 11 years, was well till she was 9 years old. It was then noticed that she was losing the power of walking, her arms were becoming weak, and she had difficulty with her speech. The disease slowly progressed, so that eighteen months later she was unable to stand or walk, and unable to feed herself. The impairment in speech had not increased. There had been no vomiting and only occasional headache. She had had some pain in the lower part of her back and in the neck. She was a well-nourished, healthy-looking child of fair intelligence, easily pleased and somewhat emotional. The upper central incisors were notched, and the spleen could be felt below the costal margin, but there was no other evidence of congenital syphilis.

Her articulation was slow and drawling, but all her words were easily understood.

She could move all her limbs well and her muscular power was good. There was no wasting. There was a very marked intention tremor of both upper and lower extremities. The child could only stand and walk with support, and even then the gait was wildly ataxic. There was tremor of the head and shaking of the trunk. When at rest there was no tremor.

There was no optic neuritis or atrophy, and no nystagmus. The pupils reacted to light and on accommodation. The knee-jerks were distinctly increased, the arm-jerks were brisk. There was no patella or ankle clonus. The plantars gave most variable responses, more often flexor than extensor; sometimes no response could be elicited. When last seen in December, 1905, she was in the same condition.

Another case is that of a boy who is still under observation :—

Case 7.—H. K., aged 21 (1905), is the second of three children, one brother two years older, and one sister three years younger; both are quite healthy. The father is healthy, the mother was an epileptic and died of general epileptic convulsions when 36 years old.

The boy was like other children till he was 13 years old. He had had convulsions when cutting his teeth, and again had a fit when 4 years old.

When 13 years old he began to suffer from fits, and at the same time it was noticed that he became unsteady in his gait and staggered about. The condition gradually increased, definite epileptic fits occurred at long intervals, but were controlled to a considerable extent by bromide.

During the earlier years of the affection he was under my care as an out-patient, and at that period he would walk into the room with a wildly ataxic gait, so that he seemed constantly in danger of falling; but he never fell. He had most marked inco-ordination of the hands, and an irregular jerky articulation. He was of normal intelligence, and not depressed about his complaint. The knee-jerks were active, there was no ankle clonus, and the plantar reflexes could not be obtained. There was no nystagmus and no spinal curvature or bony deformity of the feet.

His condition steadily got worse, so that when 19 years old he was admitted to the National Hospital under the care of Dr. Ormerod. He was a small lad for his age, and was easily pleased. There was no nystagmus or ocular defect, and the optic discs were normal. There was marked inco-ordination of both arms, so that he could not with any accuracy approximate the finger to the nose. In the legs there was marked inco-ordination, but no wasting or weakness of muscles. The knee-jerks were active and equal; there was no ankle clonus and no response could be obtained from the plantar.

He was seen again some two years later (viz., August, 1905), and he was then in much the same condition, though his gait, if anything, was less ataxic than on the previous occasion. The knee-jerks were still active, there was no ankle clonus, and the plantar reflexes could not be obtained. The disease had made little, if any, progress.

The foregoing cases illustrate three clinical varieties of ataxia which are found in children, and at any given period in the course of the disease, these three varieties may so closely resemble one another, clinically, that it is impossible to distinguish them from one another, and it is only by the history of an acute or gradual onset in a previously healthy child, or a history of congenital weakness, that the varieties can be clinically distinguished. The prognosis in the first

two varieties (*i.e.*, the congenital cerebellar ataxia, and the acute cerebellar ataxia) is comparatively good, whilst in the third (progressive cerebellar ataxia) the prognosis is bad.

Instances of the various types above described occur scattered in medical literature under various headings. The cases of congenital ataxia are, for the most part, placed under the heading of cerebral diplegia, or hereditary and family spastic paraplegia, as by Cestan and Guillain (6), who quote the observations of Pelizaeus and Dreschfeld. From the pathological findings in Mlle. Pesker's case (7), since there is affection, not only of the fibres in connection with the cerebellum, but also of the cerebrum, it would seem that there is considerable justification for such a classification.

Congenital Cerebellar Ataxia.

The typical case of congenital cerebellar ataxia is one in which the ordinary symptoms of cerebral diplegia do not exist. There is no rigidity of the limbs, but rather hypotonia of the muscles, the knee-jerks are brisk, there is no ankle clonus and no definite and persistent extension of the big toe. The course of the affection is such, that in the most favourable cases almost complete recovery takes place, or more accurately, almost complete normal development takes place. In Collier's article on "Cerebral diplegia" (8), after mentioning the choreic and athetotic movements which occur in these cases, and which he states never improve, he refers to movements resembling disseminated sclerosis, and gives an instance in which such movements slowly developed after pneumonia, in a child aged 7 years; such a case would belong to my third group of ataxia in children, in which, with or without acute illness, symptoms gradually present themselves. Warrington and Monsarrat (5), in their paper on the arrested development of the cerebellum, give an excellent résumé of the subject; their classification is based on the probable pathogenesis, and includes five groups. (1) Complete absence of cerebellum. (2) Cerebellum congenitally small, but histologically normal. (3) General sclerosis, often following acute disease. (4) Atrophy, due

to primary vascular disease. (5) Primary atrophy of cerebellar cortex. Although the clinical grouping which I have adopted cannot altogether fit in with the pathological classification of Warrington and Monsarrat, yet it is probable that cases in my group (1) "congenital cerebellar ataxia," correspond with cases in their groups (1) and (2). Cases in my group (2) acute ataxia, "encephalitis cerebelli," correspond with their group (3), whilst cases appear in my group (3), "progressive cerebellar ataxia," which also appear in Warrington and Monsarrat's groups (2) and (5).

It is well known that great deficiency of the cerebellum may exist without any marked symptoms, though, in the majority of cases, motor and mental symptoms occur, and Ferrier (9), in his article on "The Regional Diagnosis of Cerebral Disease," gives a table of cases of cerebellar atrophies from 1879-1895 which bears this out.

No case that I can find, which has been pathologically examined, corresponds, clinically, with the typical case of the first group which I have described, viz., a child who is ataxic from birth, gradually loses the ataxia, and develops, practically, into a normal child. As I have already pointed out, in the case examined by Mlle. Pesker (7), we possess pathological evidence of the condition present in cases of congenital ataxia which do not show any tendency to improvement.

Acute Ataxia.

With regard to the second group, "acute ataxia," this term was first used by Leyden (10) for ataxia of acute onset in a patient, aged 22, in whom, eight weeks after an injury, there was marked ataxia of the limbs, without loss of power or loss of ordinary sensation, but with loss of the appreciation of different weights—a difficulty in speech and attacks of giddiness. The patient did not improve.

Westphal (11) observed cases in which clinical features closely resembled disseminated sclerosis, but with this difference, viz., that the symptoms occurred acutely following on small-pox and typhoid.

Lenhartz (12) described ataxia occurring after acute disease, and gives an account of a boy, aged 8, who, after

an acute attack of dysentery, became unconscious and developed acute ataxia, from which he gradually recovered in about one year.

Whipham and Myers (13) describe two cases in which nervous sequelæ, and among them ataxia, followed on variola. They give also a digest of nineteen cases in which nervous sequelæ followed on small-pox or other acute illness; all of these except one occurred in adults.

From the somewhat large mass of literature I have endeavoured to pick out those cases which most closely resemble those described in this paper, with special reference to children.

Shephard's case (14). A child, 5 years old, taken ill at the same time as her sister with scarlet fever, became speechless and ataxic. Recovery gradually took place, so that in fourteen weeks she was again able to walk.

Feith's case (15). A child, 5 years old, developed typhoid, became completely unconscious and recovered after four weeks with aphasia. She then had marked ataxia without any disturbance of sensation, and in three months recovered completely.

Scheper's case (16). A child, 8 years old, developed measles with coma, lasting three days; on recovery there was inability to speak, marked ataxia of the limbs without paralysis, no sensory disturbance and no sphincter trouble. Speech gradually returned, but was nasal and monotonous. The memory was defective. Complete recovery took place.

Hammarberg's case (17). As a child was quite well till 7 years old, when he had cerebral inflammation with cerebellar symptoms. At first there was continuous oscillation in limbs and trunk followed by ataxia. Movements were slow and uncertain. Speech was at first lost, then returned and was indistinct and scanning. This patient remained normal till the age of 24. Then he developed delusions, had fits of mania, had some epileptic attacks and died. Atrophy and sclerosis of the cerebellum was found, with patches of sclerosis in the frontal lobes and in the left olive. Macroscopically, the vermis appeared normal; but microscopically no part was normal, the part of the vermis most affected

being the post-lobules. The pia mater was thickened all over the cerebellum.

Spiller (18) gives an account of four cases of cerebellar disease, in three of which the disease was certainly congenital, and the patients remained in a defective condition.

In the fourth case, the following early history is given, which renders it uncertain whether the disease should be regarded as congenital or acquired. The patient was the fourth child of healthy native-born parents. No instruments were used at his delivery, which was at full term. As a babe he had a weak back and did not learn to walk until he was 3 years old. When 5 years old he had an attack of scarlet fever and diphtheria, which interfered with his speech and walking. His gait showed a slight stagger, and the feet were raised very high from the ground. He died when 19 from tuberculosis.

At the autopsy it was found that the corpus callosum was defective, the cerebellum small, and the left cerebral hemisphere atrophied. Sclerosed areas were present in the cerebellum with thickened vessels. Atrophy of inferior olives, and of the middle peduncle of the pons and pontal nuclei, was present.

In discussing the position which this case holds with regard to that described by Marie, Nonne and others, he concludes that it should be regarded as a rare type of that described by Marie, although heredity could not be established.

The paper discusses the relation of cerebellar disease to the symptoms produced, and is furnished with a most useful list of references.

Lüthje (19), in a paper on the acute cerebral and cerebro-spinal ataxia, describes three cases of ataxia following typhoid fever in three children of one family, aged 10, 9 and 6. The course of the disease varied in intensity with these children, being least marked in the youngest, who completely recovered in two months, whereas the recovery of the eldest was not complete in four months. There was a period of unconsciousness from which on recovery there was marked affection of speech, very marked ataxia of the arms

and legs, with increased knee-jerks, ankle and patella clonus, but without any disturbance of sensation except stereognostic sense. The other two cases were similar, but the affection of stereognosis could not be demonstrated. Lüthje recognises two forms of ataxia, (1) the pure cerebral form; (2) the cerebro-spinal form; and he lays special stress on the affection of stereognosis as indicative of the cerebral form.

The pathological evidence in support of this form of acute ataxia being due to cerebellar disease is extremely deficient; the case recorded by Hammarberg, and possibly that recorded by Spiller, being the only evidence which can be adduced in favour of this view.

Clinically, those who favour the view that the ataxia is of cerebral origin, bring forward the loss of consciousness, the affection of speech, the mental attitude and the loss of stereognostic sense, which is present in some of these cases, as indicative of a cerebral lesion.

Those who favour the view of the cerebellar origin of the disease point to the character of the ataxia affecting the legs and trunk muscles especially, the absence of loss of power, the hypotonia of the limbs and the character of the reflexes. The affection of speech is rather an affection of articulation than of "speech," and the scanning, monotonous and jerky character may well be the result of defect in co-ordination of articulation. That the initial disturbance is so wide in some cases as to cause loss of consciousness will be denied by none, but it can hardly be used as an argument to prove that the ataxia is of cerebral origin.

To all who study these cases, it is obvious that no line can be drawn separating the cerebellar cases from the cerebral, but in certain cases the cerebellar symptoms predominate, whilst in others the cerebral symptoms are most manifest.

And it may here be well to point out that under the term cerebellar is included not only the cerebellum, but also the cerebellar peduncles in their course to the red nucleus of the opposite side.

What the exact nature of the initial lesion may be still lacks pathological proof. That the lesion is of vascular origin, would seem probable from the sudden onset. Arguing

from the analogy of similar cases of acute onset, giving rise to cerebral and cranial nerve symptoms, in which pathological proof is forthcoming, it would seem justifiable to regard these cases as similar in origin to acute anterior poliomyelitis and polio-encephalitis, and this is the view I have taken in a paper published in the *Medical Soc. Trans.* (20). That is to say, the cerebellar symptoms are due to a thrombosis occurring in the finer vessels of this region.

Progressive Cerebellar Ataxia.

With regard to the third group, progressive cerebellar ataxia, there is no doubt that these cases are nearly allied to the disease known as "Friedreich's disease," and to the hereditary cerebellar ataxia of Marie and Sanger Brown, the close relationship of which, pathologically, has been shown in a recent paper by Lewellyn Barker (22).

One of the most typical cases of progressive cerebellar ataxia, is that reported by Donald Fraser (3), in a brother and sister. The boy was healthy at birth, and when 3 years old unsteadiness was first noticed, and when 6 years old the reeling was very marked. Up to the age of 30 he was able to walk and do his work of delivering papers. There was no mental unsoundness, but his articulation was slow, gutteral, and hesitating.

This patient died when 33, and the following changes were found: The cortical substance of the cerebellum was little more than half the normal thickness, and there were gaps on the surface, probably caused by collections of fluid in the soft membrane. The white substance presented little apparent reduction, and in proportion to the grey substance appeared of undue thickness. The cells of Purkinje in the cortex were greatly shrunken and contorted, their processes being indefinite and altered in direction. The weight of the cerebellum was 1,260 grains, the average weight being 2,640 grains. The spinal cord appeared normal.

The younger sister of this patient was similarly affected, but the disease developed later and more slowly than in her brother. She could read fairly well. Her walking was so unsteady that she was ashamed to go out. The eyes could

only be kept steadily on an object by an effort of will, and they constantly tended to turn diagonally upwards and to the left, and she stated that it was a relief to let them go in that direction. When she lay down she became giddy, and she stated that her eyes "glisten"; while this continues she did not dare to move her head, or she would become worse. There was a feeling of nausea, but no vomiting.

One of the best recorded cases in childhood of this type, with pathological investigation by recent methods, is that of Michell Clarke (4), but even this case shows clinically many signs indicative of cerebral disease, and pathologically this is borne out by the marked affection of the pyramidal system.

A boy whose two uncles, aged 12 and 13, were said to have died of the same disease, was quite well till 7 years of age; it was then noticed that he had slight choreiform jerking of the arms and legs. His sight gradually failed. He became unstable, and his speech became affected. He was ataxic in walking and tended to fall backwards. His sight was extremely defective, no change was present in the discs. There was no actual paralysis. The knee-jerks were exaggerated, the plantar reflexes active, and Babinski's sign was present. He gradually got worse, his memory became bad and his speech more indistinct. He walked with an uncertain ataxic gait, and had a tendency to fall backwards. Both legs were rigid and ankle clonus was present. A few months later he was quite helpless, unable to sleep; his legs were drawn up and flexed on the abdomen, and he died about a year after the onset of the symptoms.

At the autopsy the brain was small. There was sclerosis of the occipital region; the cortex was paler and thinner than normal. The cerebellum was rather small, the white matter showed even greater sclerosis than the occipital lobes. Microscopically, the most striking change was seen in the pyramidal system, which was completely degenerated; sclerosis was present in the white matter of the cerebellum and scattered degenerate fibres in the fillets, superior cerebellar peduncles and restiform body.

Numerous instances of ataxia with atrophy of the cerebellum are recorded, but in most of the cases there is present

also mental defect, with corresponding change in the cerebral hemispheres, often associated with hydrocephalus.

In conclusion, short mention should be made with regard to three conditions which may give rise to symptoms closely approximating those described in this paper. These conditions are (1) disseminated sclerosis; (2) quiescent cerebellar tumour; (3) past meningitis and hydrocephalus.

(1) *Disseminated Sclerosis.*

It will be readily recognised that the symptoms closely resemble those of disseminated sclerosis, and although in many of the cases the course of the disease is not that which is met with in disseminated sclerosis, yet the clinical features of the disease are so similar that had they occurred in the adult it would be extremely difficult to exclude that diagnosis. Cases of disseminated sclerosis have been described in children both clinically and pathologically, but the pathological evidence is by no means convincing, and, from the pathological evidence collected in this paper, I am inclined to regard these cases as due to cerebral and cerebellar lesion, and not to a disseminated process.

(2) *Quiescent Cerebellar Tumour.*

The second condition which may give rise to symptoms similar to those which occur in the second group, is the presence of a tumour in the cerebellum, and it is well known that in the case of tuberculous tumour of the cerebellum all the acute symptoms may subside, and the child remain in moderate health for months if not for years. Most of these children have, however, very defective eyesight secondary to the optic neuritis and often complete blindness, and in addition usually have some degree of hydrocephalus. In the series of cases under consideration, optic neuritis, secondary atrophy and blindness were not present.

(3) *Past Meningitis and Hydrocephalus.*

That meningitis and hydrocephalus may give rise to the symptoms above described is possible, but the general well-being of the child, the absence of headache, and the absence

Instances of these various types are given, and it is pointed out that whereas in cases belonging to groups 1 and 2 the prognosis is relatively good, in the cases belonging to group 3 the prognosis is bad.

The pathology of the disease is discussed, and it is shown from the record of the published cases that changes in the cerebellum are the most constant feature in this affection, though such changes are frequently accompanied by other lesions of or lack of development in the cerebrum, pons, medulla or spinal cord.

Further research is needed to establish the above clinical classification on a pathological basis.

A general bibliography will be found in references (5) (18) (19) (23).

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of any evidence of hydrocephalus from the shape of the head, tend to negative this suggestion.

As with cerebral diplegia, three groups of cases may be recognised:—

(1) Natal or prenatal in origin with some tendency to improve as life advances.

(2) Acquired from acute disease with tendency to improve.

(3) Progressive cerebral degeneration with steady deterioration.

So with the cerebellum a similar classification may be adopted.

The tendency to improvement is however greater, and recovery more complete, whilst the symptoms manifesting degeneration are slower in development in the case of the cerebellar lesion as compared with the cerebral lesion.

Summary.

The object of this paper has been to attempt to classify certain cases of ataxia occurring in children which do not fall under well-known types of diseases.

The cases have been regarded from their clinical rather than their pathological aspect, and from their clinical features it would seem probable that the symptoms are due to lesions of the cerebellum and cerebellar peduncles. This is to some extent borne out by the pathological evidence of reported cases, but there is at the same time considerable evidence pointing to affection of tracts and portions of the nervous system other than the cerebellum.

The cases group themselves into three main divisions:—

(1) Cases in which ataxia has been noticed from earliest life, and in which there is a tendency to gradual improvement (congenital cerebellar ataxia).

(2) Cases in which ataxia has suddenly developed during the course of or after some acute illness in a child who was formerly quite healthy (acute ataxia, encephalitis cerebelli).

(3) Cases in which ataxia has gradually developed in a child who has been healthy and of normal development until the onset of the disease (progressive cerebellar ataxia).

chiefly from a histological and microchemical point of view, may perhaps throw some light on this question.

In the year 1899 I (44) published a paper on the microchemistry of nerve-cells, dealing especially with their nuclein compounds. Since that time, although with many interruptions, I have been making a comparison of the compounds found in nerve-cells with those of the cells of other organs. The similarity between the constituents of nerve-cells and those of certain gland-cells, as well as a corresponding difference from those of the cells of other organs, caused me to investigate this subject further.

(*b*) *Nissl Substance and Substances Resembling it.*

The cytoplasm of nerve-cells contains a substance to which prominent attention was first directed by Nissl, and which is commonly called the Nissl substance, Nissl granules, or tigroid. Held (15), who was the first to apply microchemical tests to this substance, came to the conclusion that it is a nucleoproteid. Besides its well-known property of staining with thiazin dyes, Held found that it is soluble in dilute alkalies, leaves a residue on peptic digestion, is not acted on by acids, is insoluble in alcohol, ether or chloroform, and gives no reaction with Millon's reagent or the Adamkiewicz's or xanthoproteic tests. It gave, however, a positive reaction for phosphorus, using Lilienfield and Monti's test. The reactions which I obtained were in the main confirmatory of the above, and where differences are seen they are discussed in my former paper. I found that it contains marked quantities of iron and phosphorus in organic combination, leaves a large residue on peptic digestion, gives a Millon reaction, is insoluble in alcohol, ether or chloroform, but is readily rendered unstainable in thiazin dyes by acids or alkalies through an alteration of its nuclein part. There is no doubt that the conclusion to which Held arrived, that this substance belongs to the class of nucleoproteids, is correct. I shall not go further into these reactions, except as to its relation to acids, which has led to a variance between Bethe (5) and Held. This substance is insoluble in acids, but can be rendered unstainable in thiazin dyes by treatment

ON THE METABOLISM AND ACTION OF NERVE CELLS.

BY F. H. SCOTT, PH.D., M.B.

Formerly Demonstrator of Physiology, University of Toronto.

With Two Plates.

I.—SOME CONSTITUENTS OF NERVE CELLS AND OTHER CELLS CONTAINING SIMILAR SUBSTANCES.

(*a*) Introduction.
(*b*) Nissl Substance and Substances resembling it.
(*c*) Use of Chromatic Material in other Cells.
(*d*) Neurosomes and Zymogen Granules.
(*e*) Nucleus.
(*f*) Interdependence of the various Constituents.

II.—ACTION OF NERVE CELLS AND HYPOTHESIS OF STIMULATION.

I.—SOME CONSTITUENTS OF NERVE CELLS AND OTHER CELLS CONTAINING SIMILAR SUBSTANCES.

(*a*) *Introduction.*

The presence of blood and lymph vessels in the central nervous system renders it certain that the cells of these organs need nourishment, or, in other words, have a metabolism, and many observers have been able to find differences in different states of this metabolism. Thus, changes have been observed as a result of activity, other changes have been found as a result of injury to the prolongations, and others even through merely removing normal impulses from the cell. These observations, not to mention the various changes known to occur as a result of different intoxications, make it clear that nerve-cells have a metabolism, but they have not cast any light on the nature of the action which is the result of such metabolism. My investigations, conducted

with acids, which dissolve the iron from all nuclein compounds. As it is the iron-holding part which gives to chromatins their peculiar staining properties, when this has been removed the chromatin no longer stains normally. Aqueous acids, especially hydrochloric and nitric, extract the iron very rapidly. Bünge (7) used hydrochloric acid in alcohol and thought this did not extract the iron in organic combinations, but Macallum (28) has shown this is largely dependent on the amount of material used. As sulphuric acid acts slower and can thus be better controlled, Macallum used alcohol to which 4 per cent. of this acid had been added. This unmasks the iron, that is, changes it from its organic combinations, which give none of the ordinary tests for iron, into an inorganic combination which gives the ordinary tests. The alcohol tends to keep the iron compound from diffusing into the liquid, but even in this fluid if the treatment be prolonged, the iron dissolves out of the tissue. This is especially true of such combinations as occur in the Nissl substances which give up their iron readily, so that if the treatment be prolonged they show an absence of iron, while the chromatin of the nuclei still show a marked reaction. It should be noted, as Macallum (28) has shown, that the above treatment unmasks the iron only in particular combinations. There are many combinations it does not affect. Thus it does not unmask the iron of hæmoglobin or hæmatin. This is also true of the ammonium sulphide reaction for iron, which is, however, a far more general test than that derived from the use of acid alcohols.

As the function of the Nissl substance is unknown, I thought that an examination of other cells for the presence or absence of a similar substance might cast some light on its use. After first working through the various organs separately, the plan finally adopted was to attach to the same coverslip sections of the same thickness of the different organs which had been treated in the same manner. The sections of the different organs were thus tested at the same time. A number of fixing fluids were tried, but the following were most used: Alcohol in various percentages, Carnoy's mixture, or a solution of sublimate half saturated in water, to

which $\frac{1}{10}$ of its volume of formalin, and $\frac{1}{100}$ of its volume of acetic acid were added before use. Toluidin blue with a counterstain of eosin or erythrosin was the combination most frequently employed. They were sometimes applied as Held uses them, but most frequently the sections were first stained in toluidin blue, and then differentiated in dilute erythrosin in water or alcohol. If the thiazin dye were employed alone, the sections were differentiated in dilute acetic acid (1-1000). In employing the reaction for iron a 2 per cent. sulphuric acid in absolute alcohol was used. The sections attached to the cover were left in this fluid for about four hours at 50°, and after washing in absolute alcohol, treated according to Macallum's (29) method in a pure hæmatoxylin solution. After five to ten minutes in this solution the sections were washed in alcohol, and sometimes counterstained in dilute eosin. In digestion experiments, only material which had been fixed in alcohol was employed. The sections attached to the coverslip were digested in a pepsin hydrochloric acid (0·3 per cent.) mixture for a varying time at 38° C, washed and stained in iron-alum hæmatoxylin without any differentiation.

On applying the above methods (stains, solubilities, digestion, tests for iron and phosphorus) to the cells of other organs, I find the only other places where a substance is found in the cytoplasm with similar properties, in quantity comparable at all to that found in nerve cells, are those cells which form the strong proteolytic ferments for secretion, that is, in the chief cells of the fundus glands and in the pancreas cells. In these cells it is confined to the outer striated zone, and to a much less extent in the strands of cytoplasm between the zymogen granules of these cells. The only cells where there was any difficulty in deciding as to the presence or absence of such a substance were those of the serous salivary glands, where basal filaments of a chromatic nature have been described [Solger, Müller, Garnier (12)]. These structures, no doubt, represent a somewhat similar substance, but the amount, under ordinary conditions, is so small that their occurrence has actualiy been doubted by Maximow (35). By the use of pilocarpine it is possible, as

Langley (21) has shown, to produce an outer zone to these cells, and this outer zone then shows the presence in fair amounts of a somewhat similar material, which, however, does not give as marked iron or phosphorus reaction as the substance found in the pancreas or fundus cells.

In looking for this substance organs were used from the dog, cat, rabbit, frog and other amphibians, including *Necturus*. In the cells of the liver, spleen, kidney, suprarenal, testis, epididymis, prostate, thyroid, skin glands, mucous glands, muscle or tendon, I have never met with any such substance. Cells containing combinations of mucic or chondromucic acid stain metachromatically with thiazin dyes, and the undifferentiated cytoplasm of these cells may show slight traces of iron, but such cells can readily be distinguished from cells containing a substance similar to the tigroid of nerve-cells. One has only to stain a section from the fundus of the stomach taken in active digestion to see that the chief cells contain this peculiar substance, while it is entirely absent from the parietal cells and other cells of the organ. The figures show the result of treating sections of a few of the organs with some of the methods. As I was looking for a particular substance and not for morphological details, thick sections (about 10 microns) were most frequently used. In such sections it is usually not possible to make out with certainty any details as to the structure of the cytoplasm. The figures with the same numeral were drawn from sections which had been treated at the same time. Thus figs. 1 represent (*a*) a pancreas cell, (*b*) a liver cell, (*c*) a parotid cell, and (*d*) a leucocyte from a lymph gland of the same dog. Figs. 2 are those of a chief cell and a parietal cell from the fundus of a rabbit. Figs. 5 show the distribution of iron in the same cells. Figs. 3 and 6 are from amphibian organs, and show in one case the effect of toluidin blue and erythrosin, and in the other the distribution of iron. Fig. 6*c* is a red blood corpuscle of a frog drawn from a blood-vessel in the same section from which 6*a* was taken. Figs. 7 show the result of digestion with pepsin and hydrochloric acid on sections from the same organs from which figs. 1 were drawn. A nerve cell has been drawn

Plate I.

1a

1b

1c

1d

2a

2b

3a

3b

3c

4

Bale & Danielsson Ltd lith

Plate II

5a

5c

5b

6a

6b

6c

7a

7c

7b

7d

8a

8b

Blair & Donaldson, Imp. Inst.

instead of a leucocyte. After digestion there is, in the cytoplasm of all cells, a small amount of undigested material (plastine, Carnoy), but it is a minimum compared with that left in the cells of the three above-mentioned organs. The figures show that this peculiar chromatic substance of the cytoplasm occurs only in the places indicated. It is, however, not merely a case of this substance occurring in the cytoplasm of these cells and in the nucleus in the other cells, for the basichromatin of the nucleus has other properties from this material. Thus it is much more resistant to the action of acids and alkalies, and stains readily with methylgreen, which has, as usually employed, little or no affinity for the tigroid substance of nerve-cells, or the basal region of gland-cells.

I have found only two others who have made a systematic examination of other organs for such a material as the Nissl substance. Both were made some years ago and depended solely on the use of methylene blue. Benda (3) says :—" However, granular structures staining intensely with methylene blue also occur in gland cells, liver cells, pancreas cells, salivary gland cells, tumor cells (sarcomata), and are especially numerous in normal and pathological preparations of blood forming organs, the lymph glands." Eve (11) says: " No substance with the same affinity for methylene blue is present in tendon, muscle, nerves, pituitary body, pancreas, suprarenal, ovary, kidney and thyroid."

The contents of the dog's submaxillary gland and of the chief cells of the cardiac gastric glands, and the matrix of cartilage have a similar affinity for methylene blue, but differ in other respects. The liver cells of rabbit, pig, winter frog and worm commonly contain a granular material, staining similarly with methylene blue.

Benda has evidently not distinguished between the methylene blue staining material of the nucleus and that in the cytoplasm. A material staining intensely with methylene blue is especially abundant in lymph glands, but it is the basichromatin of the nucleus. In the cytoplasm it, at best, would occur only in the basophil granular cells which are very rare. Both of these authors mention the liver cells

as containing such a substance. I have repeatedly looked for such a substance, both with methylene blue and other methods, in the liver cells of the dog, cat, rabbit, pig, frog, *Amblystoma*, *Diemycylus*, *Plethyodon* and *Necturus*, and have never found it. The granular material of which Eve speaks might be a part of the second nucleus which is common in liver cells, or it might be due to the staining of the ordinary granules of liver cells by the use of an unsuitable staining solution. By varying the method of use, methylene blue can be made to stain many things of very different nature. An old solution of methylene blue is alkaline, and gives a very diffuse stain. In sections of nervous material, not only does the Nissl substance stain, but the entire section is blue, and it is not easy to differentiate even in alcohol, but may be in dilute eosin or in dilute acids. When properly stained (32) with thiazin dyes, it will be seen that the only other gland cells in which a material with similar properties to the Nissl substance occurs are in those cells in which the proteolytic ferments are formed for secretion, and this distribution may be confirmed by the other tests. As this material occurs only in the outer zone, and to a much less degree in the strands of cytoplasm between the granules, the amount of this substance in these cells varies greatly with the stage of digestion. In the cells of a fasting animal none or very little of this substance is found, because the entire cells are loaded with zymogen granules. In the amphibian pancreas, even after three or four days' rest, there is frequently a little of this substance left. It frequently has a peculiar twisted appearance compared with the remainder of the cytoplasm, and corresponds to the Nebenkern of Nussbaum (39). I shall not go further into the morphology of this Nebenkern, but proceed with the function of the cytoplasmic chromatin.

(c) *Use of the Chromatic Material in other Cells.*

It has been known for some years that the outer zone in some ferment-secreting cells stained with nuclear dyes. Macallum (30), as a result of his observations of such cells in rest and activity, came to the conclusion that: "The chromatin of the nucleus gives rise to a substance which we

may call prozymogen . . . and which finally diffuses into the cell protoplasm, uniting with a constituent of the latter as zymogen." Later Macallum (28, 31) showed that this prozymogen, which occupies the outer zone of the cell, contains iron and also phosphorus. Mouret (37) takes a similar view that this chromatic material of the cytoplasm is converted into the zymogen granules, and calls it prezymogen. Similar views as to the use of the chromatic material have been taken by Prenant (43), Mathews (34), Garnier (12), Cade (8), and others. The failure of certain authors, *e.g.*, Pirone (42), to observe the "basal filaments," even in the fundus cells, is due to the use of the triacid staining mixture, the methylgreen of which, in the ordinary solutions, has little or no affinity for nucleins of this class, while it has for the nuclear basichromatin. Figs. 1*a* and 3*c* represent pancreas cells in activity stained with toluidin blue and eosin. Fig. 8*a* shows the hæmatoxylin reaction for iron in such a cell, while fig. 8*b* shows a cell from an animal after four days' fast. It will be seen that as the zymogen granules increase, there is a corresponding decrease in the substance which gives the iron reaction.

In his work on the histology of the gastric glands Bensley (4) confirms the observations as to the presence of such a substance in the chief cells, and mentions methylene blue as one of the suitable dyes to distinguish the ferment-forming cells, on account of its affinity for the prozymogen. He says: "It will be seen from the foregoing that there are two salient features in the structure of the body of the gland, namely, the presence of granules of zymogen in a portion of the cell of varying extent next the lumen, and the presence in large amount in the protoplasm of the outer end of the cell, and in that between the granules, of a kind of chromatin called prozymogen, which stains strongly with hæmatoxylin and other nuclear stains, and gives, after treatment with acid alcohol, a strong reaction for iron." We thus see that nerve cells have in common with these ferment-forming cells a large amount of highly organised iron-holding nucleoproteid in their cytoplasm, the Nissl substance corresponding in its characteristics to the prozymogen of Macallum.

(*d*) *Neurosomes and Zymogen Granules.*

Nerve cells have also the second great distinguishing feature of ferment-forming cells, for they also contain an acidophile granule corresponding to the zymogen granule. Altmann (1) in his "Elementar organismen," described and figured the cytoplasm of nerve-cells with a granular structure like that of other cells. In 1896 Levi (24) by using Galeotti's method (fixing in Hermann's fluid, staining much like Altmann but followed by methylgreen) found an increase of these fuchsinophilous granules after activity. It is to Held (16), however, that we owe an adequate description of the presence and distribution of these acidophil granules in nerve-cells. Held has shown, not only by Altmann's method, but with many other fixing fluids, that these granules which he calls neurosomes are in every nerve and nerve-cell, but are particularly abundant in the axis cylinder end arborisations around the body and dendrites of other nerve-cells. In thin sections it is easy to confirm Held's observations as to the presence and distribution of these granules. In the body of the cell they appear as small round or elongated granules occurring between the Nissl granules in the meshwork of the cytospongium (fig. 4.) In the processes they occur in the meshes of the spongioplasm, and often appear as thickenings of the latter. The neurosomes may be demonstrated with many methods, such as erythrosin and methylene blue, but it is more convenient to use Altmann's method or the bichromate method of Held, which give specific stains to these granules. Altmann's method also gives a specific stain to the zymogen granules of the pancreas—the outer zone being free from any such staining material. If this method merely makes precipitates of proteid from the cell sap, then the granules should also occur in the outer zone as well as in the inner, where they may be seen during life. It is not only by the use of such fixatives and stains that the neurosomes may be seen. They may be seen in isolated cells [Arnold (2)]. Turner (48), by means of a modified methylene blue solution on fresh material, has shown that the protoplasmic processes are surrounded by the

ends of collaterals or other nerve branches. These ends contain numerous varicosities which are, I believe, caused by heaps of neurosomes. Held (17) has also shown with methylene blue that these granules are abundant in the nerve endings in muscle.

The properties of the neurosomes and those of the zymogen granules are similar in their main features. The only list of properties of zymogen granules I have been able to find is that of Langley (22), for the granules of the œsophageal glands in the frog. He found the granules were dissolved in acids, less readily in alkalies, in bile almost instantaneously. Alcohol dissolved them partly. They are not soluble in glycerine or in a saturated solution of sugar The granules are not affected by a 5 per cent. potassium or ammonium bichromate solution, but they disappear from the gland cells when small pieces of tissue are left in these fluids. Besides these, they reduce perosmic acid slightly, and are visible in teased preparations. Macallum (28) has also shown they give the ammonium sulphide reaction for iron and contain phosphorus (31). They do not, however, give the hæmatoxylin reaction for iron.

My work was done entirely with the granules of the frog's pancreas, and had the double object of determining their solubility, and of trying to determine why these granules are not preserved in ordinary fixing solutions. Small pieces of fresh pancreas were either left in large quantities of the fluid, or the pancreas was left in a moist place for a couple of hours, and then a small piece laid on the slide and gently pressed with a cover. Large numbers of the granules are forced to the edge of the tissue, and the fluid may then be run under the cover, and the effect watched under the microscope. In sodium chloride (0·6 per cent.) the tissue may be left for four days without any diminution in the number of the granules. Distilled water leads to a disintegration of the granules, but whether there is a real solution is hard to determine. There is a residue left. The same remarks apply to the action of acids which lead to a disintegration. The granules may be left for four days in sodium bicarbonate (2 per cent.), or in lithium carbonate

(saturated), or in potassium hydrate (0·5 per cent.). The granules are insoluble in glycerine (four days), but are entirely digested with pepsin and hydrochloric acid. The above reactions, along with those of Langley, show that it is not so much the solubility of the zymogen granules which makes them disappear from the cells in ordinary fixatives, but partly because they are destroyed from osmotic differences, and partly because being so loosely attached to the cytospongium, they are discharged by the contraction of the cells.

The reactions of the neurosomes were determined partly with fresh tissues, but also in material which had been fixed in alcohol. The fresh material was put into the fluid to be tested, and then afterwards fixed in Altmann's fluid or in bichloride. The neurosomes are not soluble in alkalies or glycerine, are altered in acids, but disappear entirely with pepsin and hydrochloric acid. They give, after thorough extraction of the sections (5 microns) first with boiling alcohol and then with ether, a reaction for phosphorus. They do not give the acid alcohol, hæmatoxylin reaction for iron. The ammonium sulphide reaction was not tried. I should add that these reactions were obtained in the neurosomes around the Purkinje cells of the cerebellum.

It is thus seen that the neurosomes correspond in most of their solubilities and reactions to the zymogen granules of the pancreas, and of the œsophageal glands. They perhaps do not reduce perosmic acid to the same extent, and are not as visible in the fresh condition as zymogen granules. It is hard to see the neurosomes in a fresh condition owing to the myelin which tends to make everything homogeneous, but it is probable that it is a lecithin combination which gives to zymogen granules their characteristic appearance, and there is no other organ which contains so much of this substance as the central nervous system. The neurosomes can however be seen in isolated cells [Arnold (2)].

The neurosomes are, morphologically, homologous with the zymogen granules of gland cells. It may be, perhaps, a common feature of all cells to store up their products of metabolism in a granular form, and, considering these

granules, as I believe most histologists do, as products of metabolism, and not as primary living substance, it is evident that the properties of the granules will be dependent on the characters of the intervening cytoplasm where the granules are formed. When we make comparisons we find that nerve-cells, chief cells of the fundus glands and pancreas cells are classified together and distinguished from other cells of the body by having this intervening cytoplasm impregnated by a similar iron holding nucleoproteid.

(*e*) *Nucleus.*

As the nucleus is the centre of metabolism, no account of the structure of cells would be complete without reference to it, and here again we find these three cells classified together. The character of the nucleus in mammalian nerve-cells is well known. It differs from an ordinary nucleus in containing very little of what is usually termed chromatin. With methylene blue alone only the nucleolus stains, but if a counter stain of eosin be added there is also seen to be a large amount of eosinophilous material—the oxychromatin of Heidenhain. The nucleolus is also seen to have an oxyphile centre. As the oxychromatin stains, although lightly, with acid hæmalums and some other nuclear stains, little difference is seen after these stains between the nucleus of a nerve-cell and those of ordinary cells. The oxychromatin also gives a reaction for phosphorus and a slight reaction for iron, and yet there is a fundamental difference between this substance and the basichromatin of the nucleolus or the Nissl substance, for the oxychromatin is completely dissolved in pepsin and hydrochloric acid, while the basophil material is not. This shows that Mann's (33) objection to the terms "oxy" and "basi" chromatin, on the ground that they are both nucleins, is not justified; for if a nuclein is a compound which leaves a residue on peptic digestion, then the oxychromatin is not a nuclein. The latter remark will also apply to the zymogen granules of gland cells.

The character of the nucleus in pancreas cells varies con-

siderably with the stages of digestion. If one examines the cells in ordinary stages of activity, and there is much prozymogen in the cytoplasm, the character of the nucleus resembles closely that of a nerve cell. All the substance in the nucleus is oxychromatin, except for one or two small masses of basophil material collected around the nucleolus like that of a nerve cell, and perhaps one or two small masses in the remainder of the nucleus (figs. 1*a*, 3*c*). If, however, the cells are at rest, and the cytoplasm is loaded with granules, and there is little prozymogen in the cytoplasm, then the nucleus contains much more basophil material. This relation may be seen in the two figs. 8 which represent the distribution of iron in the two cases. While the nerve-cells of adult mammals and most classes of animals have much nucleoproteid in the cytoplasm and little in the nucleus and thus resemble pancreas cells in activity, it is interesting to note that the Urodela have a reversed condition, and have little or no Nissl substance in their cytoplasm, but much basichromatin in their nuclei [Levi (25), Scott (44)], and thus resemble gland-cells in rest. A similar condition to these Urodela cells is found in the cells of embryo mammals where, as the tigroid develops, there is a disappearance of the primary chromatin of the nucleus [Scott (44)].

The nuclei of the chief cells of the fundus glands of the stomach present the same features as those of the pancreas cells. When there is much prozymogen in the cytoplasm there is little basichromatin in the nucleus but much oxychromatin, and when there is little prozymogen in the cytoplasm there is much more non-digesting chromatin in the nucleus.

(*f*) *Interdependence of the Constituents.*

In the case of these gland-cells we know there is an interdependence between the amount of chromatin in the nucleus, the amount of prozymogen in the base of the cell, and the number of zymogen granules present. These facts may not prove that the iron-holding chromatin of the

nucleus gives rise to the iron-holding prozymogen of the cytoplasm, which is, in its turn, metamorphosed into another iron-holding compound—the zymogen granules; but they at least make it probable. In case any one may doubt the value of these microchemical reactions, I may point out that Nencki and Sieber (38), working with gastric juice obtained from a Pawlow's fistula in a dog, confirmed and extended the earlier observations of Pawlow and Frau Dr. Schoumow-Simanowski, that on cooling the juice to zero a fine granular precipitate is obtained. This precipitate, which contains the ferment, contains iron and phosphorus, part of the latter as a lecithin-like body, and part as a nuclein-like body.

A transformation of the Nissl substance into the neurosomes has also been established, or, at least, an interdependence between the amount of the Nissl substance and the number of neurosomes been observed. Activity in nerve-cells leads finally to a diminution of the Nissl substance, although there is probably at first a slight increase in its amount. For some of the recent work on this question see Guerrini (14), Carlson (9), and Holmes (19). Levi (24), on the other hand, has shown that there is an increase in the number of neurosomes (fuchsinophilous granules) during activity, an observation which has been confirmed by Motta-Coco and Lombardo (36). I have made some experiments which will be more fully described later, and, I believe, both of these statements are correct. The anomaly that activity leads to an increase in the number of neurosomes, while in gland-cells it leads to a decrease in the number of zymogen granules, is apparent only because we do not examine a nerve-cell in its entirety, but only the body of the cell, while it is evident that the most important point of activity is the nerve ending where a transference of energy takes place. In the long rest of hibernating animals there is, however, a marked diminution of the Nissl substance [Levi (26), Legge (23)], and corresponding to the disappearance of this substance in fatigue we find also in pancreas cells that excessive activity is also accompanied by a disappearance of the chromatic material in the cytoplasm [Dale (10)].

II.—Action of Nerve Cells and Hypothesis of Stimulation.

If we consider the result of the activities of these three cells we also find there is much resemblance between their actions. Ferments and other catalytic agents have, in all probability, only an accelerating action on changes which ordinarily proceed slowly in the substance on which they act [Ostwald (41)]. The definition of a ferment given by Oppenheimer (40) is: "Eine katalytisch wirkende Substanz, die von lebenden Zellen erzeugt wird und mehr oder minder fest an ihnen haftet, ohne dass ihre Wirkung an den Lebensprocess als solchen gebunden ist; die Fermente sind im Stande chemische Processe auszulösen, die auch von selbst, wenn auch im langsamerem Verlaufe, einzutreten bestrebt sind. Das Ferment selbst bleibt bei diesem Process unverändert. Es wirkt specifisch, d.h. jedes Ferment richtet seine Thätigkeit nur auf Stoffe von ganz bestimmter structureller und stereochemischer Anordnung." An acceleration of changes which ordinarily proceed slowly is also the action of a nervous impulse on another cell. It is also interesting to note that these two forms of activity (ferments and nervous impulses) while ordinarily leading to a decomposition may possibly, under certain conditions, have the opposite effect and lead to a synthetic combination of simpler substances.

Since proteids are the essential part of living matter it is, no doubt, by an alteration of the proteids in that part of the cell where the impulse acts that the whole cell is awakened to activity. There are thus three cells in the body whose function is to control the changes in proteids beyond their own immediate substance, and they not only have this similarity of function, but also similarity of chemical constituents. Do these resemblances mean anything, or is it a coincidence that similarity of function should also be associated with similarity of composition? These similarities have, I believe, a deeper meaning, because all life processes in cells must have a chemical basis, and as all cells in the body are derived originally from one cell, it is probable that

cells with similar function would be differentiated along similar lines as regards their chemical constituents. It must be admitted that our methods of distinguishing substances in cells are still very coarse, yet when we do make comparisons with the methods at our disposal we find that the pancreas and its cells, although morphologically resembling the parotid and its cells, has far more chemical resemblance to the glands of the fundus, to which its function has also more physiological resemblance. As the nucleus is the centre of metabolism, it is probable that in all cells it sheds some kind of a chemical substance into the cytoplasm, and as proteolytic and other ferments have been found in all organs, the diffuse blue stain which the cytoplasm of all cells gives with toluidin blue might indicate the presence in slight amounts of prozymogen, although more probably due to an oxidizing or other atom group. On whatever the peculiarity rests the fact remains, that those cells which form and secrete ferments for the destruction of proteids are classified together, for in them an iron-holding nucleoprotèid accumulates in large amounts in the cytoplasm. Seeing that nerve-cells have great resemblance both in their chemical constitution and in their action to these cells, and believing that the nervous system is something more than a mere system of conducting paths, I formed the hypothesis that nerve-cells are true secreting cells, and act upon one another and upon the cells of other organs by the passage of a chemical substance of the nature of a ferment or proferment from the first cell into the second; and that a stimulation of the latter is made through a partial destruction of the proteid constituents of the second cell where the impulse acts. The nature of the alteration or destruction produced by this substance is, I believe, very similar to that which occurs in the ordinary digestion of proteids. This hypothesis has to do with the stimulation of cells, and not with conduction which proceeds in the substance between the neurosomes; nor has it anything to do with the ultimate action of the stimulated cell which acts according to its own nature and may, as in muscle, use chiefly carbohydrate. When the impulse reaches the

nerve ending it causes, I believe, the discharge of some of the neurosomes which are very numerous in that situation, and which have, I consider, the same relation to the proferment that the zymogen granules in gland cells bear to the proferment of those cells.

In this place I shall not discuss this subject further than to point out that just as irritability and conductivity are not identical so there is, in all probability, a difference between conductivity and the process of excitation of the next cell. Many physiological facts show that although nerve-cells may touch and appear continuous with certain technique, yet they are as distinct centres of metabolism as any other two cells of the body. The action of curari, nicotine or apocodeine, or the fact that a nerve like the vagus or cervical somatic will make physiological connection with the sympathetic, all show the metabolic distinctness of every neurone. Perhaps a fact showing more clearly the independence of nerve-cells is that electrical variations will pass from the dorsal to the anterior root, but will not go in the reverse direction, even if the excitability be heightened with strychnine [Hermann (18), Gotch and Horsley (13)]. This seems to me to be clear evidence that nerve-fibres or fibrillæ are not continuous. The hypothesis of Bethe (6) that the electrical variations increase in the natural direction of conduction, while there is a great decrease in the reverse direction, is negatived by such numbers given by Gotch and Horsley (13). Their numbers show that the conduction is accompanied by the same electrical variation in both directions in the same fibre, but, whenever the impulse passes a synapse, there is a great change. Not only is there this change in the amount of the variation, but there is also a change in the rhythm [Schäfer and Horsley (45)]. This physiological independence of nerve-cells seems to me to show that the process of conduction in one cell to its synapse and the stimulation of the next cell are probably entirely different properties of the neurone. When the changes which constitute conduction reach a synapse it might stimulate the next cell by electrical variations, surface tension changes [Schäfer (46)], or by an alteration in the ionic concentration

or other purely physical phenomenon, but the retention and reactivating of such changes is a difficult matter to conceive; and yet the sensations gathered by the sensory nerves are in some manner retained in the central nervous system. Whether the known power of proteids to absorb and retain proteolytic ferments and keep them indefinitely in a passive condition until again brought into a suitable medium, throws any light on the manner in which nerve-cells retain and reactivate the stimuli they have received remains for future investigation.

We thus see that my facts derived from histological study as well as the known facts of neurophysiology, point to a close analogy between the secretion of ferments by the fundus glands and the pancreas and the process of excitation occurring in each synapse of every chain of neurones which is in a state of excitation. Just as in ferment-forming cells we have nucleus, prozymogen and zymogen, so in nerve-cells we have nucleus, pro- or Nissl substance and neurosomes. The process of excitation, like that of secretion, involves, I believe, the discharge of neurosomes in the region of the synapse. Since discharge into other cells means the using up of formed material, it must be an exhaustible process, and the process of complete recovery at the synapse must depend on the integrity of the connection of the synapse with the nucleus and cell body which are the original seats of formation of the material involved in the activity. Of this relation I have experimental evidence, as well as direct evidence, showing the independence between the conducting property of nerves and their power of exciting other cells. These I hope to embody in another paper.

Summary.

A substance of the same nature as the Nissl substance of nerve-cells occurs only in the cells of the pancreas and in the chief cells of the fundus glands of the stomach.

The neurosomes of Held are morphologically homologous with the zymogen granules of gland-cells, and there is an interdependence between the amount of Nissl substance and

the number of neurosomes exactly as there is between the prozymogen of Macallum and the number of zymogen granules.

The nuclei of these three cells also resemble one another.

There is also much resemblance in the action of these three cells in that they all are concerned in controlling the changes in proteids.

On the above similarities the hypothesis was formed that nerve cells also act by a kind of proteolytic ferment.

Explanation of Plates.

Note.—*All figures were outlined with the aid of a camera lucida. Throughout a Zeiss 2mm. apochromatic objective with ocular 4 were employed.*

Plate I.

Figs. 1.—*a.* pancreas cell; *b.* liver cell; *c.* parotid cell; *d.* leucocyte from a lymph gland. Dog. Alcohol 96 per cent. Toluidin blue, erythrosin.

Figs. 2.—*a.* chief cell; *b.* parietal cell; fundus gland. Rabbit. Alcohol 96 per cent. Toluidin blue, erythrosin.

Figs. 3.—*a.* anterior horn cell, frog; *b.* skin gland, *Amblystoma* larva; *c.* pancreas cell, *Diemyctylus*. Bichloride. Toluidin blue, erythrosin.

Fig. 4.—Purkinje cell, cerebellum, showing the end terminals (filled with neurosomes) of other cells ending around the cell. Dog. Bichloride. Toluidin blue, erythrosin.

Plate II.

All the cells here represented are stained for iron, except the series, 7*a*, *b*, *c*, and *d*, which have been digested in pepsin and hydrochloric acid, and then stained with iron-alum hæmatoxylin. The colour obtained is usually black: but on this plate all the drawings have been printed in blue.

Figs. 5.—*a.* chief cell; *b.* parietal cell; *c.* mucous cell; fundus gland of rabbit. Alcohol 96 per cent. Acid alcohol four hours and then hæmatoxylin.

Figs. 6.—*a.* anterior horn cell, frog; *b.* skin gland, *Amblystoma* larva; *c.* red blood corpuscle, frog. Bichloride. Acid alcohol 4 hours and then hæmatoxylin.

Figs. 7.—*a.* pancreas cell; *b.* liver cell; *c.* parotid cell; *d.* nerve cell from cortex. Dog. Alcohol 96 per cent. Digested twenty hours in pepsin and hydrochloric acid at 38°. Iron-alum hæmatoxylin without differentiation.

Figs. 8—*a.* pancreas cell in activity; *b.* pancreas cell four days after feeding. *Diemyctylus*. Bichloride. Acid alcohol four hours, hæmatoxylin.

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THE ONSET OF HEMIPLEGIA IN VASCULAR LESIONS.

BY A. ERNEST JONES, M.D., M.R.C.P.
Assistant Physician to the Dreadnought Seamen's Hospital.

INTRODUCTION.

THE studies on which this paper is based owe their initiation to a suggestion of Sir William Gowers, to the effect that the *post-mortem* records at University College Hospital should be investigated with a view to ascertaining the facts as to the occurrence of the different varieties of hemiplegia in the sleeping or waking state. In the course of the work it has seemed to me worth while to analyse other points noted in the records; some of the results thus obtained will be here incorporated and compared with conclusions based on other sources of information presently to be referred to. The precise clinical diagnosis of the vascular lesion in a given case of hemiplegia thus brought about is rarely a certain one even yet; this diagnosis is a necessity before a reliable prognosis can be given, and also yields valuable indications as to treatment. Its practical importance is evident when one recollects that one-twentieth of all the deaths in this country last year were due to such lesions.

METHOD.

The points of value in the diagnosis of a recent case of hemiplegia are not very numerous, and to elucidate the truth as to their significance it is useless to refer, as is often done, to clinical experience alone. There is but one method, namely, to study statistically a large and consecutive series of cases that have been investigated before and after death. Such opportunities of personal investigation are rare, at least as far as an adequate series is concerned, so that I have been impelled to work along the lines indicated in this paper.

A knowledge of the numerous fallacies to be avoided has necessitated such pruning of the material that the results attained seemed very disproportionate to the labour expended; they are, however, perhaps worthy of record for the assistance of future workers.

I feel the necessity of prefacing a few remarks on the study of hospital notes, for it is a method of study that has undeservedly fallen into discredit. This has come about because it has been generally recognised that it is one which is singularly open to fallacy; these fallacies are not, however, inevitable, as is often supposed, and after their careful avoidance this method may yield information of considerable value and otherwise inaccessible. A few words, therefore, will not be out of place here on the nature of these fallacies. They fall into two main groups: *first*, those due to the selected nature of the material under consideration, and, *secondly*, those due to errors in the process of recording the facts. Such errors may come from one or more of three sources; first, the failure to assign proper evidential value to each statement in the patient's history; secondly, the various mistakes which are possible in direct observation of physical signs; and, last, the erroneous interpretation of these observations. It is unnecessary to elaborate these latter points further here, though it might be well to insist on the importance of the last source of error, especially in the influence that it exerts on the actual observation and description of physical signs. A crude instance of all three fallacies would be the following case. A patient says that he has never had a paralytic stroke, though twelve months ago he had a bad fainting attack; some stiffness of the right arm only is found, and is ascribed to senile osteo-arthritis, the characteristic signs of the latter affection being described; after death a small clot is seen pressing on the left internal capsule.

The sources of fallacy that may be placed in the first group are, on account of their subtlety, more often overlooked. Consideration of any such material as the present series of cases at once shows that it has undergone a number of selections through various influences. Thus,

before drawing any conclusion on a given subject, as for instance the age at which cerebral hæmorrhage most often occurs, we have to remember that we are dealing, not with a consecutive series of cases of cerebral hæmorrhage, but with only those cases of this lesion that present hemiplegia as a symptom; not even with a consecutive series of hemiplegias due to cerebral hæmorrhage, but with hemiplegias due to this lesion that die, and which die in a busy hospital. Further, the conditions that influence admission to this hospital are numerous, such as proximity of dwelling or employment, rank in life (which in the lower classes is often a question of age as many of the oldest people tend to drift to the infirmary), time of day or night, &c. So that in stating any conclusion it is essential to find out first how it may have been affected by any of these selective factors. In many instances these factors may be directly measured, in others their influence may be estimated more or less approximately; when this cannot be done, they must be so incorporated in such a manner as to qualify the conclusion formulated.

Material.

A study has been made of all the cases of hemiplegia that died in University College Hospital between the dates of its foundation and the accession of the present staff. This period extends over about sixty-five years, during which time there were in use about seventy beds for adult medical cases. The cases selected have been those of vascular lesion only. Other causes of hemiplegia, such as tumour cerebri, traumatic and inflammatory lesions, have been excluded, as have also cases where the *post-mortem* diagnosis was unsatisfactory or indeterminate, such as local cerebral atrophy, cerebral sclerosis, cerebral congestion. In all there are left 160 lesions, which occurred in 139 patients; 123 were cases of hæmorrhage, 24 of thrombosis and 13 of embolism. These numbers of course in no wise indicate the actual relative frequency of the

conditions mentioned, a problem which I do not intend to discuss at present. The fewness of the cases is a little remarkable in a hospital having a rapid transfer of patients, and is in part due to the number that had to be excluded. This illustrates the very great difficulty that exists in taking notes which will be useful for research, unless the questions raised by the research are known beforehand and therefore specially investigated.

Occurrence of the Accident.

(1) *Relation to Exertion.*

It is now recognised that it is exceptional for any of these lesions, even hæmorrhage, to occur during great exertion, and that the importance formerly attributed to this factor was much exaggerated. In only one or two of the cases now under consideration was the lesion preceded by any severer exercise than that involved in walking the street. Nor do we find that this was so in more than ten of Gintrac's 840 cases (1), recorded between fifty and a hundred years ago, at a time when clinicians were especially possessed with the importance of this factor. Natural acts involving effort, such as defæcation and coitus, used to be regarded as much more dangerous in this connection than they are now held to be. Neither was mentioned as having any relation to the onset in the present cases. On an average, ten minutes of the twenty-four hours are spent under such circumstances as might lead to an attack of cerebral hæmorrhage that occur in these ten minutes being attributed to the act of defæcation; ten minutes being a hundred and forty-fourth part of twenty-four hours, then at least five of Gintrac's 840 cases should have been so attributed, even if such attacks occurred under these circumstances no more frequently than at other times. But, in fact, only two of his cases are said to have been brought on by defæcation, and these were specially recorded on account of this feature; so was also the only attack occurring after coitus, an attack that took place on the patient's wedding night. Similar comment applies to

the factor of mental excitement, which was noted in only nine of Gintrac's cases, and in none of the present series.

But if it does not seem necessary often to invoke severe exertion as the determining cause of cerebral hæmorrhage in a patient whose miliary aneurism is approaching the bursting point, there is on the other hand some evidence, as we shall see when dealing with the subject of rest and sleep, to shew that in such patients the variations of blood pressure that obtain in normal life are sufficient in themselves to precipitate the grave event. Sudden change of posture may be of importance in causing such variations in patients whose compensatory vaso-motor mechanism is failing. And there is in this series a considerable group of cases of hæmorrhage with a history to the effect that the stroke took place within a few minutes of getting out of bed.

(2) *Relation to Rest.*

If these lesions occurred with equal frequency during rest and customary exertion, and if the particular patients spent as much time in bed as other people, then we might expect to find that about a third of the attacks took place in bed. The facts are these :—

	Number of cases with point noted.	Percentage occurring in bed.
Hæmorrhage	114 ...	18·4
Thrombosis	22 ...	31·8
Embolism	13 ...	54·6

Now, are there any reasons why any of these lesions should enter this series in such a way as to raise its "bed percentage?" There are excellent grounds for believing that hæmorrhage kills much more quickly than either of the other two, and we may suppose that cases of rapidly fatal hæmorrhage occurring in bed at night would be less likely to be brought to the hospital than similar cases taking place in the daytime, while, for instance, the patient was at work But the number of cases that are fatal in a few hours is very small, so that we need raise our bed percentage for such cases only by a little, say, to 20 per cent. The next possible fallacy is the likelihood of any of these cases occurring in

individuals who spent more time than usual in bed, *i.e.*, who were invalided from some cause or other. As regards hæmorrhage, this was operative to a certain extent. Of the ten attacks of hæmorrhage that occurred in hospital, five did so while the patient was in bed. Again, of the twenty-one cases in which hæmorrhage took place while the patient was in bed, five had suffered from a previous attack of hæmorrhage and one from cerebral thrombosis. Some of these previous attacks had occurred years before, and these would incapacitate to a less extent than more recent ones. Still, on the whole, we may assume that quite 40 per cent. of the twenty-four hours were spent in bed by the hæmorrhage patients, taking 30 per cent. as the normal proportion. And as only 20 per cent. of such attacks took place there, this definitely suggests that rest in bed to some extent protects against hæmorrhage.

Taking now *thrombosis*, the average age of these patients was less than that of the hæmorrhage ones, and there had been no prior attack or immediate illness in any of the cases, so that the time spent in bed by such patients was approximately normal. As less than a third of the thrombosis attacks took place during rest in bed, we have then no reason to suppose that such rest makes thrombosis either more or less likely to happen than moderate exertion.

As regards *embolism*, most of the patients had, of course, heart disease, a potent cause of confinement to bed. All the four embolisms that occurred in the hospital occurred while the patient was in bed, thus illustrating this point. With the limited data at our disposal, it is impossible to estimate this factor, so that it is also impossible to comment on the relation of rest to embolism.

(3) *Relation to Sleep.*

The amount of time spent in sleep is on the average greater in persons who spend more time than usual in bed, though how much so we do not know. We must, therefore, consider the subject of sleep in relation to that of rest in bed.

In the present series there are :—

	Number of cases with point noted.	Percentage with onset during sleep.
Hæmorrhage	110 ...	9·9
Thrombosis	22 ...	22·7
Embolism	11 ...	27·3

In other words, thrombosis occurred during sleep more than twice and embolism nearly three times as often as hæmorrhage. Comparing this sleep incidence with the bed incidence, we note that of the hæmorrhage and embolism attacks that occurred in bed one half did so while the patient was awake, whilst this was only true of one-third of the thrombosis attacks. What, now, is the proportion of time that similar patients usually spend awake in bed?

Dealing first with *hæmorrhage*, we have to remember at the start that the sleep incidence would doubtless be raised could we include the cases which die at home during the night, though, as we remarked above, this increase would probably be but slight. We also saw that patients in whom hæmorrhage occurred probably spent rather more time in bed than those who suffered from thrombosis, though less than those in whom embolism occurred. They would differ from the instances of embolism in sleeping rather more than normal individuals, for one of the causes of confinement to bed was a previous hæmorrhage, and this, when recent, would be likely to bring about stupor. On the whole, we might expect that they slept for quite three-quarters of the time they spent in bed, altogether then for about 30 per cent. of the twenty-four hours. Yet we find from reference to the above table that, instead of 30 per cent. of the attacks occurring during sleep, less than 10 per cent. did so. This strongly suggests that sleep protects against cerebral hæmorrhage to an even greater extent than rest in bed. This protection that sleep seems to afford is illustrated by the facts that of the ten attacks that took place in the hospital only two came on during sleep, and of the fourteen cases of repeated attacks only one occurred during sleep. Different authorities usually state either that the occurrence of cerebral hæmorrhage during sleep is very rare, or that it is very

common. On the one hand, Dana (2) says that if a person finds that he is hemiplegic on waking in the morning we may assume pretty safely that the lesion is thrombosis and not hæmorrhage, as supposed cases of hæmorrhage occurring during sleep usually turn out to be thrombosis. On the other hand, Charcot (3) says that in infirmary work he found that hæmorrhage most often occurred, not merely in bed, but during sleep and at night. Sormani (4) held the same opinion, but in this instance it was not founded on cases examined after death. Vlantassopoulo (5) summarises three factors in his statement that hæmorrhage occurs "either during sleep, or more exactly at the moment of waking, or else in the first hours that follow rising, this being perhaps due to the changes in the hydraulic conditions of the cerebral circulation." Thevenet (6) says that this statement is endorsed by most clinicians to the extent of being supposed to possess some diagnostic importance. Such contradictory statements, based on no consecutive series of cases, show the danger of generalising from personal impressions. The only consecutive series I know of is Gendrin's (7). Out of 176 cases in which cerebral hæmorrhage was found *post mortem*, in 97 (or 55 per cent.) it had occurred during sleep, and in 84 of these during the night sleep. The great divergence of the present results from those of Gendrin appears in several of the points investigated, and cannot be explained completely, even by the selection of his cases from the aged infirm. My results harmonise better with those of Tooth (8), who found that of 246 attacks of hemiplegia in 19·1 per cent. the onset was during sleep; unfortunately, the diagnosis of the lesion was not verified in these cases, and, no doubt, in a number of them it was thrombosis.

Turning now to *thrombosis*, we saw that there was no reason to suppose that these patients differed much from normal people in the time they spent either in bed or during sleep. The figures then suggest that sleep did not in itself make thrombosis more likely to occur; indeed, as far as they go, they point rather in the other direction. This is not necessarily antagonistic to such statements as that of James Taylor (9), to the effect that one of the commonest condi-

tions under which thrombosis occurs is during profound sleep, for he refers in this connection to very old people who have recently suffered great fatigue, and the present series of thrombosis cases was not composed of the senile invalids commonly taken to be the kind of patients who suffer from this affection.

As regards *embolism*, the evidence is much more equivocal, on account both of the smallness of the numbers and the unknown influence of confinement to bed. In spite of this confinement, heart cases are not notoriously good sleepers, so that we might expect quite half of the time spent in bed to consist of waking hours. The figures thus give no reason to suppose that sleep predisposes to or protects against embolism. Of the four attacks of embolism that occurred in the hospital only one did so during sleep.

(4) *Time of Onset.*

On this subject also very contradictory assertions have been made. Charcot (3) said that *cerebral hæmorrhage* occurred most often in the late hours of the night; he gave no figures in support of this. Sormani (4), basing his statement on several thousands of cases, said that there were two especial times of the day when the accident occurred, one between two and four in the morning, the other between three and five in the afternoon. I suspect, however, that these cases were obtained from the official returns of the Italian Registrar-General, to whose department Sormani belonged, and that the lesions were not verified. Dana (2) says that morning and evening are the times of election, the accident being rare in the middle of the day. On the other hand, Gendrin (7) gives details of the precise time of ninety-three cerebral hæmorrhages inspected after death, and in this series nearly two-thirds of all the attacks took place within four hours, namely those between midday and two p.m. and midnight and 2 a.m.; in other words, the precise opposite of the times given by the other authorities. Gendrin's results are most extraordinary, and are not confirmed by any other observer; they serve, however, to cast

doubts on statements based on less exact data. Of the present series the exact hour was given in sixty-two instances, and the approximate hour in forty-two, making 104 in all.

	Gendrin.	Mushet.	Present Series.	Total.	Percentage.
Noon to 2 p.m.	26	1	9	36	19·8
Midnight to 2 a.m.	31	1	2	34	18·7
2 to 7 a.m.	8	1	11	20	10
7 to 12 a.m.	5	0	16	21	11
2 to 8 a.m.	9	3	25	37	20·3
8 to 12 p.m.	14	1	19	34	18·7
Total	93	7	82	182	

In the above table Gendrin's series is given, together with the present one, and a small series of Mushet's (10); all the cases were verified after death.

If we consider the present series first, of ninety-two cases only nineteen occurred at night (between midnight and seven a.m.), while seventy-three occurred in the other hours; in addition, two cases occurred in the "morning" and ten in the "evening," so that the preponderance of day over night is even more marked than appears in those figures. Half the cases occurred between ten in the morning and five in the afternoon, a seventh between five and eight in the morning, an eighth between nine in the evening and midnight, and a tenth between six and eight in the evening. Four-fifths of the cases, then, occurred in the first three of these periods, namely, at midday, in the rising hours of the morning, and in the late evening, which would seem in these instances to have been the elective times. The purely relative value of these data, however, is shown by a glance at the accompanying table, which reveals the entire discordance between my results and those of Gendrin. Thus, of his cases over 60 per cent. occurred in the four hours following midday and midnight, whereas only 13 per cent. of the present cases did so; again, only 24 per cent. of his cases occurred between two and twelve p.m., whereas 54 per cent. of the present cases did so. The chief conclusion to be drawn then is that definite statements such as Dana's and

Charcot's must be regarded with some doubt. The onset would seem to be determined by such variable factors that the time of day is in itself of little interest, as is the time of year, although much significance has been ascribed to both of these.

As regards *thrombosis* and *embolism* similar remarks apply, but I will give shortly the main facts gleaned from this series. The time of onset was stated in twenty cases of thrombosis and thirteen of embolism, precisely in four of these and eight of those. In both instances nearly half the attacks occurred in the middle of the day (between nine a.m. and three p.m.), about the same proportion as in those of hæmorrhage. But, whereas only 11 per cent. of the hæmorrhage attacks were in the early morning (between one and six), in thrombosis and embolism the percentage incidence was 30 and 38 respectively. The tendency to dwell on the importance of the early morning in relation to occluding lesions should be checked, however, by the knowledge of the limited extent of the data.

The Symptoms of Onset.

The precise initial symptom was not stated often enough in such a manner as to render a summary of the records of any value on this point. In a general way it may be said that they strongly confirmed the current teaching as to the frequence of nausea or *vomiting* at the onset of cerebral hæmorrhage, and its comparative uncommonness in other vascular lesions, a fact first insisted on by Sir William Broadbent (11) thirty years ago. Twitchings and *convulsions* were commoner with the occluding lesions than with hæmorrhage, and were more often met with when the cortex was affected. General convulsions occurred in nearly a third of the embolism cases; this was so within twenty-four hours in twenty-four out of ninety-seven cases recorded by Eliza Walker (12), but in only seven out of seventy-two recorded by Newton Pitt (13). The last observer's series included an unusually large number of latent embolisms, which the other series did not. Convulsions may occur in cerebral hæmorrhage apart from either meningeal or intra-

ventricular bleeding, though they are more frequent under these circumstances. Of thirty-six cases of intraventricular hæmorrhage recorded by Thomas Jones (14), there were convulsions in four only, which accords with the present observations. Hirtz recorded seventy-seven cases of hæmorrhage that showed convulsions, and in fifty-five the blood was intraventricular.

Loss of consciousness is important in that often it is regarded, whether rightly or wrongly, as one of the main aids to diagnosis. For instance, Trousseau (15) attached such value to this that he asserted that preservation of consciousness at the onset of the attack excluded all idea of a hæmorrhage. Jeannin (16) similarly lays down that there is *always* loss of consciousness with cerebral hæmorrhage. Yet we have Leandier (17), in his article on cerebral hæmorrhage in Bernheim's System, saying that the apoplectic onset of this affection is less frequent than a gradual onset with no loss of consciousness. Again, Vlantassopoulo (18) insists that the cases that recover have for the most part not been accompanied at the onset by the least trace of loss of consciousness.

It is not common to get an accurate description of the initial symptom from a bystander, but it was mentioned as consisting in immediate loss of consciousness in two cases which did not prove to be primary intraventricular hæmorrhage, as cases showing loss of consciousness as the initial symptom are usually said to be. It is well known how emphatic Trousseau's (19) dictum was on this point, namely, that such descriptions if carefully investigated *invariably* reveal some earlier symptom than loss of consciousness.

I shall consider here only the subject of loss of consciousness occurring within a short time of the onset; terminal stupor and coma are, of course, almost invariable, which is one of the reasons why ingravescent coma of late onset is of such sinister omen.

(1) *Relation to Lesion.*

It seems to be generally accepted that *occluding lesions* cause loss of consciousness less frequently than does hæmor-

rhage, and that such loss is less profound and lasts for a shorter time. This statement, first ascribed to Todd, and emphasised by Lancereaux (20), is repeated by Nothnagel (21), Monakow (22), and most writers on the subject. Saveliew (23), on the other hand, in an exhaustive work based on 191 cases of cerebral embolism, says that *most* of such patients lose consciousness, though often for a short time only, and that preservation of consciousness is relatively rare. I do not know of any series in which have been systematically investigated the intensity and duration of the coma, or the correlation of the phenomenon with the intensity or even the existence of paralysis. Some facts bearing on the frequency of coma are given here. Consciousness was lost in ten out of twenty-two cases of *thrombosis*, and in six out of thirteen of embolism; in neither instance did this loss bear any relation to the site or extent of the lesion. Of thirty-four cases of *embolism* collected by Gintrac (24), eleven showed loss of consciousness. Of sixty collected by Thevenet (25), twenty-one showed it; of these twenty-one, eight were carotid or basilar embolisms, and two more were cases of simultaneous blocking of both Sylvian arteries, so that only eleven out of fifty single embolisms in arteries other than the carotid or basilar caused loss of consciousness. Incidentally this emphasises the importance of these two arteries in relation to this symptom. Newton Pitt's (13) four cases of basilar embolism showed no symptom except loss of consciousness. Consciousness was lost in twenty out of thirty-three cases of embolism collected by Lancereaux (26), and clouded in several others. It was lost in three out of Jeannin's seven cases, and in forty-five out of sixty-four cases of Eliza Walker (12), being slightly impaired in eight more of these last. Of the total, then, of *201 cases* of embolism, consciousness was lost in at least 47·7 per cent., while it was affected in nearly 60 per cent. This tallies, as it happens, with the figures relating to embolism given in the following table.

Turning now to the subject of *cerebral hæmorrhage*, we find that consciousness was lost early in eighty-nine of 111 cases in the present series, *i.e.*, in over 80 per cent. This

agrees fairly well with the figures given by Thomas Jones (14), 72 per cent. of thirty-six cases, and Gintrac (27), 69·3 per cent. of eighty-eight hæmorrhages into the brain substance; there was loss of consciousness in only 38 per cent. of the purely cortical hæmorrhages described by the latter writer. Of these 235 cases taken together, consciousness was lost in nearly 75 per cent. In the table of the cases included in the present series, I have considered hæmorrhage under two headings, intraventricular and extraventricular; the former was nearly always secondary. It is worthy of note that consciousness was retained till near the end in four cases in which there was *post-mortem* evidence that a considerable quantity of blood had been present in the ventricles for some time. One of these patients lived for five days. There is a case of Charcot's (28) on record where the patient recovered and lived for six months in this condition, and Rokitansky has published similar cases.

	Number of Cases.	Percentage with loss of consciousness.
Ventricular Hæmorrhage ...	55	85·5
Non-Ventricular Hæmorrhage ...	49	69·4
Thrombosis	22	45·5
Embolism	13	46·1

It is likely that the percentage is heightened a little by the fact of the cases being taken from the records of a busy hospital to which unconscious patients would be likely to be brought. The figures illustrate the two ways in which a clinician may be misled by attaching undue importance to the phenomenon, namely, by overlooking the existence of the following two classes of cases. On the one hand, there is a large group—certainly more extensive than shown in this table—of cerebral hæmorrhage cases having the onset typical of thrombosis, and on the other, there is a large group of thrombosis cases the onset of which is apoplectiform. This latter group, first recognised by Rochoux in 1812, has been carefully described by Durand-Fardel (29) in his monograph based on 181 cases of cerebral softening. He says that 58 per cent. of his cases presented this mode of

onset, a considerably higher proportion than is seen in the series now recorded. There is no exact evidence as to which of the above groups is the larger; Tooth (30) refers to the former as being so. Some writers still maintain, as Copland (31) insisted, that the onset of paralysis, followed later by an apoplectic attack, means thrombosis. As a matter of fact, however, there is a special type of cerebral hæmorrhage of which this occurrence is equally characteristic; similarly ingravescent apoplexy occurs at times with thrombosis, and not only with hæmorrhage as Copland taught.

It will thus be seen that our positive knowledge on this subject is not great, and a series would prove of great interest in which was studied accurately the incidence of the phenomenon and its relation to such features as the intensity of the paralysis, the extent and site of the lesion, &c.

(2) *Relation to Age.*

Durand-Fardel (29) said that the apoplectiform variety of onset of thrombosis was the more likely to occur the older the patient. In his series, of twenty-nine such attacks only eleven were below sixty and one below twenty, whereas of thirty-four "gradual" onsets twenty-four were below sixty, and six were below twenty. Brissaud (32), on the other hand, says that it is in senile softening that the progressive, gradual onset is seen most often. The present series, although only a little more than a third of Durand-Fardel's in number, as far as it goes tends to support Brissaud's view. The following table is based on eighty-five cases.

		Percentage of cases below 20.	Percentage of cases above 60.
Apoplectiform Onset	Durand-Fardel ...	3	62
	Present Series ...	0	18
Gradual Onset	Durand-Fardel	18	29
	Present Series	9	27

(3) *Relation to Survival.*

Coma supervening at a late date is always of bad import; it would seem, as shown in the accompanying table, that

hemiplegia of apoplectiform onset, whatever its cause, carries with it a similar increase in the gravity of the prognosis. Of the commoner variety of hæmorrhage—the extraventricular form—more than twice as many patients died of the immediate attack when the onset was apoplectiform than when it was not so.

	No. of Cases.	Percentage dying within 24 hours.	Percentage dying within a week.	Percentage dying within a month.	With loss of consciousness. With no loss of consciousness.
Intraventricular Hæmorrhage ..	55	47	66·0	92·0	98·0	With loss of consciousness.
		8	25·0	75·0	100·0	No loss of consciousness.
Extraventricular Hæmorrhage ..	49	34	17·6	64·7	88·3	With loss of consciousness.
		15	13·3	33·4	40·0	No loss of consciousness.
Thrombosis ..	22	10	10·0	30·0	70·0	With loss of consciousness.
		12	9·3	25·0	58·3	No loss of consciousness.
Embolism ..	13	6	0	50·0	50·0	With loss of consciousness.
		7	0	14·3	14·3	No loss of consciousness.

Length of Survival.

(1) *Relation to Lesion.*

There can be little doubt but that the immediate prognosis is much graver with *hæmorrhage* than with the other two lesions, though it is an exaggeration to say, as Brissaud (33) does, that early death is infinitely rarer with softening than with hæmorrhage. As so many of the patients of the present series were admitted for the actual attack, one cannot ascertain directly the absolute frequency of recovery from these lesions; this is shown by the surprising number of hemiplegics of twenty years' standing that may be seen in our infirmaries, while of the present series no case dated further back than five years. Dana (34) says that two-thirds of patients with cerebral hæmorrhage recover from the immediate attack, which may, I suppose, be taken to last a fortnight. On the other hand, 72·5 per cent. of 109 such patients in the present series died within a week. This discrepancy may be explained in part by the fallacy above mentioned, and in part by the fact that in the period in

which the attacks occurred, the mortality from cystitis and acute decubitis was very considerably higher than at the present day. Drozda (35) studied 927 cases in the three main hospitals of Vienna, and tells us that 43·12 per cent. recovered to such an extent as to leave the hospital; the fatal cases (56·68 of the whole) were all verified after death, but of course some of the patients that recovered may have been suffering from thrombosis.

The following table shows the relative mortality in the present series :—

	Number of cases.	Percentage dying within 24 hours.	Percentage dying within a week.	Percentage dying within a month.
Cerebral Hæmorrhage	109	37·7	72·5	86·2
Intraventricular Hæmorrhage	57	59·7	89·7	98·3
Extraventricular Hæmorrhage	52	15·4	53·8	73
Thrombosis	23	8·7	30·4	60·8
Embolism	13	0	30·7	30·7

It will be noticed that when blood flowed into the *ventricles*, nearly 60 per cent. of the patients died in the first twenty-four hours. One patient lived forty minutes, another thirty and one only fifteen, recalling the oft-quoted case of Abercrombie's (36) that proved fatal within five minutes of the initial symptom. These facts clearly negative such statements as Vlantassopoulo (37), who, endorsing a remark to the same effect by Lancereaux, says that the gravest hæmorrhage, even when accompanied by ventricular or meningeal inundation, never leads to death in a time shorter than some hours. Two of the patients in this series who lived for nearly a month, and another one who survived six weeks, presented *post-mortem* evidence that a clot had been present in their ventricles throughout.[1]

Of the *extraventricular* cases, the one running the most rapid course proved fatal in ten hours; the longest course was five years. Mushet (10) has published a case of this nature that died in thirty minutes, so that this rapid course is not confined to ventricular bleeding. On the other hand, cases living for twenty years are extremely rare, whereas with

[1] *See* Case of Charcot's quoted above.

thrombosis they are quite common. Only three of Gintrac's 650 cases in which the duration of survival was stated, lived for ten years. I have compiled details from the published notes of *828 cases* in which cerebral hæmorrhage (whether intra- or extra- ventricular) was found after death, 650 having been collected by Gintrac (38), 43 by Charcot and Bouchard (39), 17 by Andral (40), 9 by Mushet (10), and 109 being of the present series. Of these 828 cases 30·4 per cent. died within twenty-four hours, 63·8 per cent. within a week, and 79·4 per cent. within a month. These percentages, although the material on which they are based is extensive, are probably rather too high, for the following reasons. They are obtained from hospitals, where the worst cases are taken; they are mostly published cases—and the special points for which they were published may often relate to circumstances of the onset, so that such a series would select against old-standing cases; and they are cases treated in the pre-aseptic era, when the mortality was unnecessarily high. On the other hand, Drozda's results, based on an even larger number, are to be much discounted by doubt as to the diagnosis of his recovering cases; in any case, his method must have caused selection of his data in favour of the apparent recovery from cerebral hæmorrhage. Summing up, therefore, it would seem probable that, even if the mild cases were included, quite half die within a week, and that a half of these die within the first twenty-four hours; whilst of the usual run of hospital cases the mortality is distinctly higher than this.

Taking now the subject of *thrombosis*, early death is certainly rarer here than with hæmorrhage. Nothnagel (41) says that there are only a few cases on record in which death took place within twelve hours; he refers here to both the occluding lesions. One of the present cases proved fatal in two hours; one, on the contrary, lived eighteen years. I have notes of *158 cases* of thrombosis, 106 being from Andral (40), 29 from Gintrac (42), and 23 being in the present series. The mortality of the whole was more rapid than in the present cases alone, while it will be remembered that in the case of hæmorrhage the mortality in the cases gathered from all sources was rather lower than in the

present series alone. Of the 158 cases of thrombosis, 1·58 per cent. were fatal in the first twenty-four hours, 38 per cent. within the first week, and 74·7 per cent. in a month. It is striking that these figures, as far as they go, shew that hæmorrhage patients die twice as often as thrombosis ones in the first twenty-four hours, whereas in a month the deaths seem to be practically the same number in both instances. That this difference in the early deaths may really be even greater than here appears is suggested from the fact that Andral's cases showed an unusually fatal tendency. Thus only two out of his 106 patients lived for a year (43), which is certainly discordant from the experience of infirmary work, where such very large numbers of these older cases may be seen.

As regards *embolism*, the problem is complicated greatly by the commonly co-existing heart disease, and that death is determined more often by the latter lesion has been well pointed out by Newton Pitt (13) and Thevenet (44); the former observer states that only 40 per cent. of the deaths in his series of ninety-five embolisms were due to the cerebral lesion. His series, however, contained an unusually large number of cases of malignant endocarditis, in many of which the embolism was not even suspected until after death. The suggestion from Pitt's series is that the occurrence of cerebral embolism increases the seriousness of the outlook by indicating the probability that the infectivity of the endocardial lesion is reaching a higher degree of virulence and approximating to the malignant variety. The longest span of life in any of the present cases was eight months after the accident. As in the case of thrombosis, a considerably smaller number of cases of embolism than of hæmorrhage succumb in the first twenty-four hours; in the present series not a single case did so. I have collected notes of *273 cases* of cerebral embolism in which the length of survival was stated, 127 having been published by Eliza Walker (12), 55 by Newton Pitt (13), 34 by Gintrac (45), 8 by Jeannin (46), 36 by Lancereaux (26), and 13 in the present series. Of these only 8 per cent. died in the first twenty-four hours, 35 per cent. died within the first week, and 56 per cent. within the first month. Of Pitt's cases

21·8 per cent. died in the first twenty-four hours, whilst of all the other series only 4·5 per cent. did so.

Lesion.	Number of cases collected.	Percentage dying within 24 hours.	Percentage dying within a week.	Percentage dying within a month.
Hæmorrhage	828	30·4	63·8	79·4
Thrombosis	158	15·8	38·0	74·7
Embolism	273	8·0	35·5	56

(2) *Relation of Survival to Age and Sex.*

I have investigated only cerebral hæmorrhage in this connection, as the numbers are too few in the other lesions. The following tables refer, the first to the subject of age alone, the second to sex alone, and the third to sex at different ages.

I.

	Number of cases.	Percentage dying within 24 hours.	Percentage dying within a week.	Percentage dying within a month.	Age.
Present series	76	36·8	60·5	85·8	Under
Collected cases ..	350	32·8	59·0	77·0	60
Total ..	426	33·3	59·3	77·9	
Present series	36	19·4	60·0	77·7	Over
Collected cases ..	327	26·6	61·8	79·2	60
Total ..	363	25·8	61·4	79·0	

II.

	Number of cases.	Percentage dying within 24 hours.	Percentage dying within a week.	Percentage dying within a month.	Sex.
Present series	85	36·5	67	83·5	Male
Collected cases ..	392	31·4	58·9	75·3	
Total ..	477	32·2	60·3	76·7	
Present series	37	24·3	48·6	75·7	Female
Collected cases ..	285	27·7	62·4	82·1	
Total ..	322	27·3	60·8	81·3	

III.

	Number of cases.	Percentage dying within 24 hours.	Percentage dying within a week.	Percentage dying within a month.	Sex.
Under 60	259	35·9	59·8	76·8	Male
	167	29·9	58·6	79·6	Female
Over 60	210	26·6	60	75·7	Male
	153	24·8	63·4	82·4	Female

These figures are too few to be at all conclusive, but the results they point to, as far as they go, are these. From the first table we see that a higher percentage under 60 years of age die in the first twenty-four hours than of those over 60, but that this difference is more than abolished before the first week is out. According to the second table, it is the men who suffer most heavily in the first day, and the mortality in women does not exceed that in men until after the first week. The third table combines the other two, and from it we conclude that the younger men die on the first day in greater numbers than in any other class; the older women, who survive the first day best, are more prone than any other class to die in the next few weeks.

Site of the Lesion.

This is a subject which has been worked out fairly fully, at all events in the case of cerebral hæmorrhage, by Andral, Gintrac, Brouardel, Drozda, and other writers. For this reason, and also because the material in the present series does not comprise sufficiently precise information on many of the necessary points, I shall not attempt to deal with more than one of these points, namely, the side of the lesion. Some other details of the present series, however, will be given, on the chance of their proving of service for further studies.

(1) *Side of the Lesion.*

It has for a great many years been taught that hemiplegia due to cerebral hæmorrhage is most often a right-sided one, whilst that due to either an occluding lesion or hysteria is

usually a left-sided one; this is often asserted to be of considerable value in diagnosis. It is interesting to observe that different writers have attempted to explain these differences by inventing quite contradictory anatomical data. Thus, Portal (47) says that cerebral hæmorrhage is more common on the right side because the right carotid is in a more direct line with the aortic stream than the left, so that the right side of the brain is more exposed to the force of the heart beats; while Rühle (48) says that cerebral embolism is more often met with on the left, because the left carotid is in a more direct line with the aortic stream than the right, so that fragments are swept to the left side of the brain rather than to the right. To account for the "paradoxical" cases of embolism on the right side, Jeannin (49) suggests that in these instances a left brachio-cephalic (innominate) artery is present, though he says that he has never been able to find a record of such an occurrence, and Cohn (50) suggests that in such cases the embolism has originated in the right innominate trunk or internal carotid artery. Without lingering any more on these ingenious hypotheses, however, let us examine the facts.

First, let us consider *cerebral hæmorrhage*. The dictum that this occurs more often on the right side has been handed down to us from Morgagni (51), who, basing his opinion on fifteen autopsies, came to the conclusion that the lesion was three times as common on the right side as on the left. Gendrin (52) went further when, from a study of forty-two autopsies on cerebral hæmorrhage cases, he concluded that this lesion was *five* times as common on the right side as on the left; this result is as startling as others of this author that we have referred to above. Larger numbers, however, tell a different story. Of 118 cases in the present series 68 showed hæmorrhage on the right side. I have collected a series of *995 cases* made up as follows: Gintrac (53), 373; Drozda (35), 282; Tooth (54), 76; Durand-Fardel (70), 117; Rochoux (56), 35; present cases, 118. Of this total number 496 showed hæmorrhage on the right side of the brain and 503 on the left. Under these circumstances the necessity of investigating the hydraulics of the aortic circulation in this connection becomes less pressing.

Turning now to the subject of *thrombosis*, we meet with a similar conflict of statements. Most authorities are agreed that the lesion is commonor on the left side, but whereas Leandier (57), writing in Bernheim's System, says that it occurs "almost always" on the left side, Andral (40) insists that it is rather commoner on the right side, and Dana (58) says that one side is as often affected as the other. In the present series of twenty-three cases, nine were right-sided and fourteen left-sided. Of a series of *176 cases*, in which the lesion was unilateral, Durand-Fardel (55) 140, Lancereaux (26) 11, Eliza Walker (12) 2, present series 23, there were eighty-three on the right side and ninety-three on the left.

It is with *embolism* that writers are most certain of the predilection of the lesion for one side. Nothnagel (59) says that it occurs "far more often" on the left side, and there are only a few authorities, such as Oppolzer (60) and Duroziez (61), who are not convinced of this preponderance, though the latter author is only sceptical on this point in cases in which the preceding heart disease is due to rheumatism. James Taylor (62) says that 60 per cent. of the lesions are left sided. Of the present cases five were on the right side and eight on the left. I have collected *558 cases* of unilateral lesions, from the following sources:—Saveliew (23) 65, Strauss (63) 22, Bertin (64) 38, Meissner (65) 32, Gintrac (45) 40, Eliza Walker (12) 117, Lancereaux (26) 39, Thevenet (66) 35, Duroziez (61) 68, Newton Pitt (13) 89, and present series 13. Only Saveliew's personal cases are counted, since his collection includes many of the cases elsewhere collected. Series such as Jeannin's (16) and Boé's (67), which were specially selected to show features in a way that would vitiate the enquiry now made, left hemiplegia being the thesis of the first work and aphasia of the second, have not been included. Of the total number 236 had right sided and 322 left, so that the percentage incidence of the latter was, as James Taylor surmised, practically 60. I know of no similar collection that contains more than a third of the numbers here given.

To summarise the above question, we may say that of 995 cases of hæmorrhage, 176 of thrombosis and 558 of embolism, a right-sided lesion was present in 49·89 per cent. of the first, 47·2 per cent. of the second, and 40·48 per cent. of the third. We have therefore no evidence in support of any predilection for one side on the part of the first two lesions, and even in the third case the evidence is not conclusive. It can be shown mathematically that when a given chance, *e.g.*, a right-sided lesion, appears 236 times in a series of 558, under such circumstances that only two options are open, *e.g.*, right and left (for all median and bilateral lesions were excluded), then all we are justified in concluding from such data is that, if a similar series were investigated in larger numbers, the chance would appear somewhere between 187 and 279 times per 558 trials; in other words, the true percentage would be, not necessarily 40·48 per cent., but some hitherto undetermined percentage, which would lie between 31·75 per cent. on the one hand and 49·11 per cent. on the other. So that, as far as we can say at present, embolism may be equally common on the two sides, or it may be twice as common on the left as on the right; and it is as likely to be the one as the other. This series does show, what no previous series that I am aware of has shown with certainty, that at all events embolism cannot be much commoner on the right side than on the left. We have further to bear in mind that most of the above series were collected by observers who were previously convinced of the partiality of embolism for the left side, and this may have affected the collecting process in some instances. It may well turn out, therefore, that embolism is in reality equally frequent on the two sides, or even more frequent on the right; it cannot be much more frequent on the right, and may turn out to be decidedly more so on the left. I do not think that we are in a position at present to make any more precise statement on the subject.

(2) *Position of the Lesion.*

Of the 123 cases of *hæmorrhage* in the present series, only five were primarily pontine, though, of course, the pons

was frequently implicated secondarily to hæmorrhage in the hemisphere. Primary pontine hæmorrhage occurred in nineteen of Tooth's 118 cases (54), in two out of 751 of Gintrac's cases (68). Cortical (non-meningeal) hæmorrhage was only present in two instances of the present series. Rupture of the hæmorrhage into the ventricles took place in fifty-two out of 109 cases of the present series in which the point was noted; this incidence, 47·7 per cent., is remarkably close to that observed by Tooth (69) in his 118 cases, where it was 47·4 per cent., but not to that recorded by Gintrac (68), which was only 6·1 per cent. of 751 cases. In the present series, blood was found in both lateral ventricles twice as often as in one alone. When found in both lateral ventricles, it was present in the third and fourth ventricles in eight-ninths of the cases. Of the eighteen cases showing blood in the fourth ventricle as well as the lateral, in only two was it present in one lateral ventricle only.

As regards *occluding lesions*, the middle cerebral artery was naturally the one usually affected, for the series was selected by the existence of hemiplegia. The basilar alone was once thrombosed, as was the artery of the crus cerebri. Thrombosis affected the cortex alone in six instances, the internal capsule alone in five, and both in eight. One, three and eight were the corresponding numbers with embolism.

Conclusions.

The most definite conclusion to which these investigations point is that we stand in great need of a large series of cases of vascular lesions, the history of which has been critically studied, and the evidences of the lesion before and after death carefully recorded. The following are the results of the present inquiry that seem to rank highest in the grade of probability, but until we have better evidence before us, they are to be looked upon as purely tentative efforts to reach the truth.

(1) Rest in bed, and especially sleep, protect to some extent against cerebral hæmorrhage. This would seem a more accurate statement than that rest and sleep predispose to thrombosis, as I can find no evidence in favour of this,

though in actual practice the two statements have a similar bearing on diagnosis.

(2) Severe exertion and time of day appear to have had too much stress laid on them in the past. A miliary aneurism that is going to rupture rarely needs the aid of severe exertion for this consummation. Time of day is only of interest when the habits of the patient's blood-pressure at different hours are known.

(3 Consciousness is lost at the onset in half the cases of occluding lesions and three-quarters of hæmorrhage lesions. It is transitorily affected in many of the remaining cases, but we have no accurate knowledge as to the depth or the duration of the coma in the various lesions, its relation to the intensity of the paralysis, or many other important questions. Until these latter are decided, it is well to remember the danger of relying too greatly on this aid to diagnosis, on account of an important group of occluding lesions in which the onset is apoplectiform, and another group of hæmorrhage lesions in which the onset is quite insidious.

(4) The immediate prognosis is much graver when the onset is apoplectiform; especially is this so in cases of hæmorrhage. Contrariwise, cases of late hemiplegia due to hæmorrhage are less likely to have suffered from loss of consciousness at the onset than hæmorrhage cases taken as a whole, and are therefore the more likely to be attributed to thrombosis.

(5) Intraventricular hæmorrhage, which is nearly always secondary, may not cause loss of consciousness. On the other hand, immediate loss of consciousness as the initial symptom may be due to extraventricular hæmorrhage.

(6) The immediate prognosis is much graver in cases of hæmorrhage than in cases of occluding lesions. In 828 cases of hæmorrhage, 158 of thrombosis, and 273 of embolism, the results are as follows: Over 30 per cent. of the cases of the first lesions were fatal within twenty-four hours, half as many of the second lesion, and a quarter as many of the last lesion; almost two-thirds of the first patients are dead in a week, and more than a third of the patients with occluding

lesions. Of twenty cases of each lesion four hæmorrhage ones would survive a month, five thrombosis ones and nine embolism ones. Most of those that survive two years are cases of thrombosis.

(7) Of the cases in which blood is found in the ventricles, 60 per cent. die in the first twenty-four hours and 90 per cent. in the first week. It is not very rare, however, for such cases to live a few weeks.

(8) The mortality incidence is heaviest on the first day amongst the younger men; in the next few weeks it is the aged women who are most likely to die.

(9) There is no indication that hæmorrhage affects the right side of the brain more often than the left. Occluding lesions may affect the left side more than the right for all we know to the contrary, but there is no evidence that is at all conclusive in favour of this supposition, and the statements commonly made on the subject are not warranted in the present state of our knowledge.

In conclusion, it is my pleasant task to offer my sincere thanks to Sir William Gowers for the kindness he has shown me in connection with this contribution; I am also indebted to the Committee of University College Hospital for permission to make use of their records.

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Reviews.

Some Recent Researches on the Tracts of the Brain-Stem.

(1) *Untersuchungen über die Leitungbahnen des Truncus cerebi.* M. Lewandowsky. *Neurobiologische Arbeiten.* (O. Vogt.) Erster Band; Zweite Lieferung.

(2) *Experimentale und Pathologisch-anatomische Untersuchungen über den Verlauf einiger Bahnen des Centralnervensystems.* S. Mingazzini. *Monatschrift für Psychiatrie und Neurologie.* Bd. xv., 1904.

(3) *Les Pédoncules cérébelleux supérieurs.* A. van Gehuchten. *Névraxe,* vol. vii., 1905.

(4) *Le Corps Restiforme et les connexions bulbocérébelleuses.* A. van Gehuchten. *Névraxe,* vol. vi., 1904.

These four papers may be grouped together for the purpose of a review of recent work on the anatomy of the brain-stem, as they all deal with structures of this region, though individual parts naturally receive more attention from the one or other author. Reference is occasionally made to other publications which tend to substantiate or controvert the conclusions of the authors under discussion.

Lewandowsky's monograph deserves close attention. This is, in the first place, due to the large amount of material on which his conclusions are based, the study of complete series of forty brains which had been subjected to experimental lesions—dogs and cats were the subjects of his experiments; and secondly, to the application of the method of Marchi, which is now almost universally admitted to be that most capable of giving positive and definite results when employed with reasonable care. If anything can be urged in adverse criticism of the work, it is that the experimental lesions appear to have been so extensive that in many instances the isolation of tracts could have been obtained only with difficulty and at the risk of confusion.

Mingazzini's work, on the other hand, results from the study of the central nervous system by Weigert's stain. His material consisted of five human brains in which destructive processes had developed during life, and of the brains of three animals on which Luciani had operated. The method he has used is of course not capable of yielding such positive results as that which is known by the name of Marchi, but in experienced hands the careful observation of the secondary and tertiary degenerations which follow local lesions may give much information on the origin and coupling up of the systems of fibres concerned.

van Gehuchten's papers bear the imprint of the careful work of their author. They result from the study of degenerations from experimental lesions in the brains of rabbits by Marchi's method.

Cerebellum.—The recent work of Clarke and Horsley (1) leads to the conclusion that none of the efferent cerebellar fibres take origin in cerebellar cortex, and that the axones of these cells only reach the central nuclei. van Gehuchten's results entirely confirm these observations, but he has not attempted, as these authors have, to determine the more precise relations between the two structures. According to Mingazzini, on the other hand, the cortex of each lateral lobe sends fibres to the opposite nucleus dentatus.

Superior Cerebellar Peduncles.—According to van Gehuchten the fibres of the superior peduncles arise from the cells of the nucleus dentatus, and probably also from those of the roof nuclei. Lewandowsky inclines to the same opinion, but has not been able to bring its definite proof. Both authors are agreed that all the fibres of this peduncle are cerebellofugal, but Mingazzini describes a considerable proportion of them as cerebellopetal. According to van Gehuchten none of the peduncular fibres decussate in the vermis, but Lewandowsky recognises such fibres, and names them the tractus uncinatus (identical with the faisceau en crochet of Russell and Thomas). The fibres of this tract arise (according to the investigations of Probst) from the cells of the nucleus tecti, and leave the cerebellum in its superior peduncle lying in its dorsal part during its course through the mid-brain. Here the tract bifurcates, the one branch, fasciculus retropeduncularis, ends around cells between the peduncle and the fillet, the other (fibræ cerebellovestibulares) passes caudalwards along the inner side of the corpus restiforme, and ends in the nucleus dorsalis acustici (? nucleus of Bechterew), and in the descending vestibular root.

The authors who have worked with Marchi's methods are in

full agreement on the extracerebellar course of the superior peduncle. Its decussation in the midbrain is complete, none of its fibres pass further oralwards than the decussation on the homolateral side. After decussation the tract breaks up into two branches, an ascending and a descending. The descending branch bends caudalwards through the pons, gradually diminishing in bulk and becoming more median in position. Its fibres seem to end in the pontine gray matter, chiefly in the nucleus reticularis tegmenti (of Bechterew), but some could be followed almost to the inferior olives (Lewandowsky). To van Gehuchten, however, it seemed that the exact termination of these fibres could not be determined. The larger ascending branch gives off fibres and collaterals to the nucleus ruber, but its chief mass enters the lamina interna thalami, and ends, according to van Gehuchten in the median portion of the thalamus, according to Lewandowsky in the nuclei ventralis a., medialis b., and nucleus lateralis anterior (of Monakow). Neither author was able to trace fibres to the other basal ganglia, to the internal capsule, or to the cerebral cortex. van Gehuchten describes a second decussation of some of the fibres of the superior peduncle in the thalamus, the one branch passing ventral to the third ventricle into the opposite thalamus, *i.e.*, that homolateral to the lesion.

Lewandowsky believes that the superior peduncles are not joined by any fibres from the nucleus ruber during their oralward course.

Neither van Gehuchten nor Lewandowsky has been able to trace a tract leaving the cerebellum by its superior peduncles to pass to the spinal cord (descending cerebellar tract of Cajal), and both have been unable to find any evidence of the neutral cerebello-thalamic tract described by Probst (5). According to Probst's first description this tract leaves the cerebellum in its superior peduncles, then turns medialwards in the tegmentum of the pons and decussates with its fellow in the raphé; it then runs oralwards dorsal to the fillet and through the capsule of the nucleus ruber to reach the neutral nucleus of the thalamus. In later publications (3 and 4) Probst described additions to this tract from the region of the spinal root of the nervus trigeminus and from Deiters' nucleus.

According to Mingazzini's views the constitution of the superior peduncles is more complicated. He admits that the majority of its fibres are cerebellofugal, but these end round the cells of the caudal end of the nucleus ruber, and from there a second link of neurones connects the system with the ventral

portion of the thalamus, and possibly a third set of fibres passes from here to the cerebral cortex. He does not recognise a descending branch of the peduncle. It also contains cerebellopetal tracts. Fibres from the cerebral cortex (from the frontal and possibly too from the temporal lobe) reach a not yet defined centre in the tegmentum which must lie oral to the nucleus ruber, and from it a second set of neurones arises which decussate with the cerebellofugal fibres, and pass to the cerebellum through its superior peduncles. The capsule of the nucleus ruber is formed by superior peduncular fibres, and fibres which arise in this nucleus join the peduncles during their decussation. Mingazzini's conclusions also tend to confirm the existence of a decussation of peduncular fibres in the cerebellum.

Sand (8) also describes cerebellopetal fibres in the superior peduncles in man as a result of examination of material by Marchi's method. According to him, however, they come from the cortex or the corpus striatum, or from both.

Middle Cerebellar Peduncles.—The information on the middle cerebellar peduncle is less definite. Lewandowsky concludes that it contains chiefly cerebellopetal fibres from the contralateral pontine nuclei, and possibly, but in smaller number, also cerebellofugal fibres to the pons, as Thomas has described. One such tract runs within the median part of the peduncle to the nucleus centralis superior internus.

Mingazzini considers the system in relation to the cortico-pontine tracts and the fibræ transversales of the pons. Cerebellofugal fibres reach the homo- and contra- lateral sides of the pons, and from here other neurones pass oralwards with the contralateral pyramidal tracts through the middle fifth of the pes pedunculi. Other cerebellofugal fibres end in the nucleus reticularis tegmenti. The descending systems consist of fibres from the frontal lobe which end in the dorsomedian cells of the pons, whence other axis cylinders spring, which pass through the strata profundum et superficiale into the opposite middle peduncle; and fibres from the temporal lobes which pass through the lateral fifth of the pes to the lateral pontine nuclei and to the nucleus reticularis; and from here a second link passes to the opposite peduncle; finally, the pyramidal tracts give fibres or collaterals to the cells of the stratum complexum pontis.

According to Lewandowsky the fibræ olivo-cerebellares are the chief constituent of the corpus restiforme. All these are afferent to the cerebellum, *i.e.*, the cerebellum does not emit any fibres to the inferior olives. As the majority of these fibres decussate in

the medulla this connection of the olives with the cerebellum is contralateral. They end in the lateral lobe, in the flocculus, and possibly too in the vermis. The tractus spino-cerebellaris dorsalis (Flechsig's tract) is also an important constituent of the inferior peduncles; it terminates in the anterior part of the vermis. The dorsal columns of the spinal cord do not send fibres directly to the cerebellum, nor do any fibres of the dorsal column nuclei reach it. Each corpus restiforme contains two descending tracts. (1) Fibres which pass down with it course round the same side of the medulla as fibræ arcuatæ externæ ventrales, and bend dorsalwards round the pyramidal tract of the same side, to end in the nucleus raphé, a small collection of cells which lies between and dorsal to the pyramids. (2) The other tract consists of the fibres to Deiters' nucleus. van Gehuchten, whose results were obtained by experiments on rabbits, concludes that the corpora restiformia do not contain any cerebellofugal fibres. Besides the direct cerebellar tract and the fibræ olivo-cerebellares they contain fibres which take origin in the bulb; of these the most important are those which arise in connection with the cells of the nucleus lateralis medullæ, and end chiefly in the homolateral side of the vermis. Other fibres take origin in the reticular formation of the medulla, the bundles can be traced from its ventral and dorsal portions—fibræ reticulo-cerebellares ventrales et dorsales. Their relation to the cerebellum is chiefly direct, partly crossed. His results agree with those of Lewandowsky to the exclusion of spinal fibres and of fibres from the dorsal column nuclei in the corpus restiforme.

Mingazzini describes two cerebellofugal systems in the inferior peduncles; the one bundle passes to the opposite inferior olive, and the other consists of fibres which decussate in the ventral portion of the raphé, and form the fibræ peripyramidales of the opposite side. They end in the nucleus arciformis. He also draws attention to the participation by the accessory olives in the distribution of the cerebellofugal fibres.

Secondary Motor Tracts.—The chief efferent spinal tracts of the cerebellar system, described by Lewandowsky as those from Deiters' nucleus, and from the nucleus ruber. The fibres from Deiters' nucleus are, after their origin, diffusely scattered through the cross section of the medulla, and first collect into a definite tract, dorsolateral to the inferior olives. In the ventrolateral columns of the upper cervical segments of the spinal cord they are still scattered, and almost surround the ventral horn in which they end; the majority are in homolateral relation with the cord,

but a small proportion decussate in the pons a short distance from their origin. As the group of cells known as Deiters' nucleus has no connection with the vestibular nerve, this tract should not receive the name vestibulospinal. Nothing new is added as to the course of Monakow's bundle. It rises from the cells in all parts of the nucleus ruber, and not from only those of an isolated region as Kohnstamm and many other observers describe. It certainly receives no fibres from the thalamus or the neighbouring gray matter. Further, it contains, as far as the available evidence goes, the only efferent fibres given off by the nucleus ruber. Preisig (2), however, from examination of retrograde tigrolysis by Nissl's method, comes to the conclusion that its anterior cells send axones oralwards, and that only the cells of its caudal half supply fibres to Monakow's bundle. After its decussation and during its course through the pons Monakow's bundle is joined by fibres from the contralateral pontine nuclei (fibræ pontospinales). Some of its fibres end in, or give collaterals to, the nucleus lateralis medullæ, but the majority enter the lateral columns of the spinal cord, and probably end in the intermediate gray matter.

The tractus tectospinalis springs from the large cells of the stratum griseoalbum medium of the anterior quadrigeminal bodies. It takes the course which has been already fully described. In the pons and bulb it gives off many fibres, especially in the direction of the facial nuclei, though it is doubtful if any of its fibres actually have this destination. Further caudalwards it fuses with the dorsal longitudinal bundle, and passing through the ventral column of the cords splits up in the ventral horns.

The dorsal longitudinal bundle is a complex system of fibres with various origins and terminations. The descending tracts are: (1) Fibres which spring from the cells of Darkschewitsh's nucleus (nucleus of posterior commissure) and run in the median part of the bundle to the level of Deiters' nucleus, below which they lie ventral to it. They enter the ventral column of the spinal cord on the same side, without having any relation to the intermediate cranial nerve nuclei. (2) The tractus pontis descendens (Probst) which rises from the large cells in the neighbourhood of the motor trigeminal root. (3) Fibres from Deiters' nucleus. The latter two systems also end in the ventrolateral columns of the spinal cord. The chief ascending tract of the dorsal longitudinal bundle consists of fibres which spring from Deiters' nucleus and terminate in the third and fourth nerve

nuclei. Probably they also provide ramifications to the abducens nucleus. In spite of previous assertions to the contrary the dorsal longitudinal bundle does not supply any root fibres to the oculomotor nerves.

Another tract which Lewandowsky mentions as ending in the third nerve nucleus is the tractus pontis ascendens described for the first time by him. It springs from the nucleus reticularis pontis or from the cells around it, decussates caudal to the decussatio brachii, and runs oralwards dorsal to the median fillet to the nucleus ruber, at the caudal end of which its fibres bend dorso-medialwards to enter the oculomotor nerve nucleus.

Hitherto, little has been known of the origin or destination of the group of fibres which in cross-section of the midbrain are known as Forel's bundle. Lewandowsky believes they have an extensive origin in the pons and medulla, some rise as far caudalwards as the inferior olives. The tract is represented by scattered fibres in the formatis reticularis medullæ, which collect into a more compact bundle ventral to the nucleus dorsalis acustici. Oralwards it takes the well-recognised course, and increases in size. It ends in the ventral portion of nucleus ventralis b. of the thalamus.

Sensory Systems.—The median fillet is another tract whose constitution has led to much discussion. From the work of Lewandowsky it would appear that it certainly does not contain any spinal fibres. It will be remembered that many text-books describe fibres from the ventro-lateral columns of the cord as one of its chief components. Probst, however, in a recent work confirms the existence of fibres of spinal origin in the fillet in man (6). Its chief source is from the dorsal column nuclei, by way of the fibræ arcuatæ internæ, all of which that enter the fillet decussate. The arrangement is such that the fibres from the nucleus gracilis go to form its lateral part, which thus contains the second link of the lumbosacral dorsal roots, while those from the nucleus of Burdach's column pass oralwards in its median portion. In the pons it receives fibres from the contralateral sensory nucleus of the trigeminus, but not from the substantia gelatinosa of the spinal root. The fillet does not give off fibres or collaterals till it reaches the level of the corpus geniculatum internum; there some of its fibres split up in a small collection of cells between this ganglion and the brachium posterius—nucleus parageniculatus. None of its fibres enter the lateral fillet or pass to either of the quadrigeminal bodies. All its fibres end in the thalamus, none pass to the basal ganglia, to the

internal capsule, or to the cortex. The majority pass through the lamina medullaris externa, to end in nuclei ventralis and nucleus ventralis anterior; a smaller number enter the lamina medullaris interna and reach nucleus medianus. Lewandowsky has not been able to find any evidence of the existence of the central sensory trigeminal tract which Wallenberg and others have described springing from the spinal trigeminal root, and he believes the fillet alone serves to conduct centralwards the sensory impressions from the face. These conclusions practically agree with those of Probst and Tschermak.

Wallenberg (9) has recently described two newly known tracts in connection with the main sensory nucleus of the trigeminus. The one consists of coarse fibres which end in motor trigeminal nuclei, in both central trigeminal nuclei and in the third nerve nuclei, but a few reach the thalamus. The other, which contains finer fibres, joins the contralateral fillet, and can be followed in it to the centre median of the thalamus.

Mingazzini concludes that the "chief fillet" contains both centripetal and centrifugal tracts. In the paper under consideration he only deals with the latter, but his arguments are inconclusive and his statements indefinite. His opinion seems to be that the chief origin of these centrifugal fibres is in the ventral nucleus of the thalamus, and their termination in the interolivary layer and the contralateral dorsal column nuclei. The so-called accessory bundles of the fillet are discussed in more detail, especially the fasciculus pontinolateralis. In the midbrain it lies ventral to the chief fillet, further caudalwards occupies its median portion, and at the level of the seventh nucleus the fibres begin to disappear, though some reach to the interolivary layer. He concludes that it springs from the cortex, and is consequently centrifugal, though it may contain centripetal fibres as well. He has not been able to decide finally if it serves in the conduction of cortical impulses to the cranial nerve nuclei, as Hoche and Theile have described.

To Lewandowsky it seems probable that all fibres which connect the pallium and thalamus are corticopetal, at least they have their cells of origin in the thalamus. The fibres which have been described as connecting the thalamus with the nucleus ruber do not exist, nor does the thalamus send any fibres to the spinal cord.

Auditory System.—The roots of the auditory nerve and their central connections have been carefully studied by Lewandowsky. The lateral (cochlear) root ends in the nucleus ventralis and

tuberculum acusticum, from which three central tracts spring, viz., the corpus trapezoides; the fibræ acusticæ of Held, which bend round the dorsal edge of the corpus restiforme, and then ventralwards through the spinal trigeminal root, to reach the homolateral olive; and the striæ acusticæ of Monakow, which decussate in the raphé, and only join the corpus trapezoides in the opposite olive. These systems form the corpus trapezoides, which enters into relation with the contralateral superior olive and nucleus trapezoides, and to a less extent with those of the same side reinforced by fibres from these nuclei the corpus trapezoides forms the lateral fillet, and it has no other connections. After giving fibres to and receiving such from its nucleus, the lateral fillet ends in the posterior quadrigeminal bodies. The commissure, which Probst has described connecting the two nuclei of the lateral fillet, is easily demonstrated. It crosses the raphé just caudal to the decussatio brachii. These are the sole terminations of the lateral fillet; none of its fibres reach Deiters' nucleus, and none pass further oralwards than the posterior quadrigeminal bodies. The next link in the central cochlear system is brachium posterius, which ends in the internal geniculate body, though according to Mingazzini, there is a direct connection between the posterior quadrigeminal bodies and the temporal lobes. The lateral root of the eighth nerve does not, however, consist exclusively of cochlear fibres. In the first place, some of its fibres pass oralwards to form a tract lying in the lateral angle of the fourth ventricle median to the corpus restiforme, which ends in Bechterew's nucleus. The name fasciculus solitarius acustici is proposed for this. A second set of fibres of the lateral root bend caudalwards to enter the descending vestibular root.

The majority of the fibres of the median (vestibular) root bend caudalwards into the descending root, others end in the nucleus dorsalis acustici, chiefly in the homolateral, partly in that of the opposite side. No direct root fibres enter the cerebellum, there is no evidence to support the existence of Edinger's "directe sensorische Kleinhirnbahn."

The nature of the cerebral root of the trigeminus still remains doubtful. Certain only is it that the axis cylinders of its large cells descend and join the motor root, but it is not yet finally settled if these are the only fibres in contains, or if ascending fibres run in it.

Another bundle of fibres, which takes origin in the region of the cerebral trigeminal root, was first described by Probst, and to it Lewandowsky suggests that this worker's name should be

applied. Probst's tract runs at first with the trigeminal root, and, after the exit of this, lies in the dorsolateral part of the formatio reticularis of the pons, in the neighbourhood of Deiters' nucleus. It ends in the gray matter, ventral to the nucleus dorsalis vagi.

The central tegmental tract certainly arises from the cells of the anterior quadrigeminal bodies, but it probably also receives fibres from the pontine nuclei in its caudalward course. It ends in the inferior olive. Probst (6), who failed to see this tract in animals, describes its origin in man from the nucleus ruber or its neighbourhood, but on unsatisfactory grounds.

The pyramidal system and cerebral peduncles contain no centripetal fibres. The greater bulk of the fibres end in the pontine nuclei, and the substantia nigra receives a considerable number. The pyramidal system has no relation to the fillet, it neither gives to or receives fibres from it, and Lewandowsky has been unable to find any evidence of the "Bündel zur Haube," or of the other accessory fillet systems which have been frequently described.

Sand (8) has come to the same conclusion from examination of human material by Marchi's method, though many fibres pass obliquely through the fillet on their way to the motor nerve nuclei. These discrepancies may perhaps be explained by Probst's observation that pyramidal fibres run in the fillet only in some brains. He describes the "Fussehleife" which lies dorsal to the pyramidal tract in the pes pedunculi, and the "Bündel vom Fuss zur Scheife," which leaves the pyramidal tract in the pes, winds round the medial border of the latter and passes dorsalwards into the fillet.

Lewandowsky has not been able to follow degenerated pyramidal fibres to the nuclei of any of the cranial nerves, though, at the level of the facial and hypoglossal nuclei fibres leave the pyramidal tracts and cross the raphé to the contralateral side. Similarly, degeneration can never be traced into the ventral horns of the cord; the myelinated fibres end in the intermediate gray matter, and they certainly do not enter Clarke's column, as Rothman (7) has suggested. Proximal to their decussation a few pyramidal fibres enter the homolateral olive, but none could be traced to the contralateral, as Probst and Rothman have described.

The tract of fibres in the lateral columns of the upper cervical cord described by Thomas and known by his name appears to Lewandowsky to take origin in the formatio reticularis of the

caudal part of the medulla. Practically all of them end in the gray matter of the cervical cord, and they thus compose a conduction system between the medulla and the latter.

The exact origin of the two spino-cerebellar tracts is uncertain. According to Lewandowsky they are homologous systems, Gowers' tract carrying fibres from the sacrolumbar, the direct cerebellar tract from the dorsocervical cord. Both spring from the cells of Clarke's column or its representatives in the lumbosacral cord, and decussate almost immediately after origin. They give fibres to the nucleus lateralis medullæ as they pass it, and enter the cerebellum, ending chiefly in its homolateral half after passing through their well recognised course. The direct cerebellar tract ends in the anterior vermis, Gowers' in the posterior vermis. No fibres leave Gowers' tract to pass further oralwards than the cerebellum. Lewandowsky failed to find any spinal fibres ascending to the thalamus or to the midbrain.

Mingazzini, in a case of microcephaly, found a considerable number of fibres in the direct cerebellar tract, though no cells were visible in Clarke's column. He therefore concludes that this tract receives fibres from other cells, and probably, too, direct dorsal root fibres, an assumption entirely at variance with all accurate observations on the subject.

GORDON HOLMES.

(1) CLARKE AND HORSLEY. BRAIN, 1905, vol. xxviii., part 109, p. 13.
(2) PREISIG. *Journal für Psychiatrie und Neurologie.* Bd. iii.
(3) PROBST. *Archiv. für Psychiatrie.* Bd. xxxv.
(4) „ „ „ „ Bd. xxxiii.
(5) „ *Monatschrift für Psychiatrie und Neurologie.* Bd. x.
(6) „ *Sitzungsber. d. Kaiserl. Akadamie der Wissenschaft in Wien.* Bd. cxii., 3 Abth.
(7) ROTHMAN. *Archiv. für Anatomie und Physiologie.* Supplementband, 1903.
(8) SAND. *Arbeiten aus dem Neurolog. Institut in Wien.* Bd. x.
(9) WALLENBERG. *Anatomischer Anzeiger.* Bd. xxvi.

The Tics.

(1) *Tics.* Henry Meige. (*Monographies Cliniques sur les Questions Nouvelles.*) Masson et Cie., Paris, 1905.

(2) *Étude Critique sur le Tic Convulsif et son Traitement Gymnastique.* Cruchet. Thèse de Bordeaux, 1902.

(3) *Bemerkungen zur Lehre vom Tic.* Oppenheim. *Journ. f. Psychologie u. Neurologie,* Bd. 1, 1902.

(4) *Discussion.* Meige, &c. *Congrès des Médecins Aliénistes et Neurologistes de France.* Limoges, 1901.

Discussion. Meige, Pitres, Cruchet, Grasset, &c. Grenoble, 1902.

Discussion. Meige, Rudler, Chomel, Dupré, &c. Bruxelles, 1903.

Discussion. Meige, Feindel, Cruchet, Rudler, Chomel, &c. Pau, 1904.

It is unfortunate that our acquaintance with the word "tic" is to a great extent limited to the term "tic douleureux," for our conception of its meaning is unconsciously coloured by our interpretation of the phenomena of that condition. Now, whatever "tic douleureux" be, in the light of present-day knowledge it is assuredly no tic. Nor can we consider it satisfactory that the cognate phrase "habit spasm" should be in vogue, especially in this country, to express those reputedly harmless "nervous movements" with which we are all familiar, for it is no less inaccurate than it is misleading, and, moreover, it is gratuitously exclusive. A tic may arise from a habit as well as from other sources, but it itself is more than a habit; on the other hand, its earliest manifestation may be a spasmodic motor reaction, but it is certainly not a spasm. To the French school of neurology more particularly is due the credit of having made an honest attempt to extricate the word tic from its uncongenial surroundings, and to restore it to its proper estate. The fact that it is found in many languages would seem to show that it has a certain specificity of meaning, while perhaps its chief recommendation is that it is non-committal.

In spite of recent advances, it is curious how indefinite medical science is in the handling of common terms such as spasm, convulsion, clonus, tremor, and it is pathetic to observe the refuge sought in the adoption of generalisations such as myotonus, myoclonus, myotetanus, myokymia, microkinesis, hyperkinesis, &c., for they only serve to obscure the issue. Uncertainty is so

frequently attributable to a confused terminology that it is desirable Meige's latest definition should be quoted in full.

"A tic is a co-ordinated purposive act, provoked in the first instance by some external cause or by an idea; repetition leads to its becoming habitual and finally to its involuntary reproduction without cause and for no purpose, at the same time as its form, intensity, and frequency are exaggerated; it thus assumes the characters of a convulsive movement, inopportune and excessive; its execution is often preceded by an irresistible impulse, its suppression associated with malaise. The effect of distraction or of volitional effort is to diminish its activity; in sleep it disappears. It occurs in predisposed individuals, who usually show other indications of mental instability."

If we proceed now to the application of this carefully-worded statement, it is plain that *a tic is not a convulsion*, in the sense that the two are not identical. Cruchet has endeavoured in his thesis to base the pathological physiology of tic on researches of Monakow *à propos* of the occurrence of choreic, epileptoid, or athetotic movements after certain lesions of the cerebrospinal axis, and to find an analogy in the action of various convulsion-producing substances. His conclusion is that tic is as often spinal as cortical in origin, that it is in short a mere symptom, common to many cerebrospinal conditions. But if tic be doomed to be used indifferently for convulsion, its retention in scientific phraseology is unjustifiable. Instead of widening its significance it is preferable to restrict it, and to employ the term convulsion in its most general sense of any anomaly due to excess of muscular contraction, of whatever variety or derivation. Thus understood, tic and convulsion are far from being synonymous, inasmuch as the latter includes the former, and many other morbid phenomena.

Further, *a tic is not a spasm*. According to the hypothesis advanced by Brissaud, which has the merit of explaining the facts without straining them unduly, a spasm is the result of sudden transitory irritation of any point in a reflex arc; it is a reflex act of purely spinal or bulbo-spinal origin. The focus of irritation may be situated in peripheral end-organ, on centripetal path, in medullary centre, or on centrifugal fibre. This conception of spasm may be enlarged by remembering that developmentally the gray matter of the cerebral convolutions is ectodermic, as is the skin, and capable of functioning as a sensory surface; it may be considered the end organ of an afferent path that conducts to medullary reflex centres. Hence irritation of a point on the

Rolandic cortex or on the cortico-spinal tracts is followed by a motor reaction; the sole change is in the route taken by the centripetal stimulus; the reflex centre remains bulbo-spinal, and the efferent limb of the arc is as before.

Now, though the application of the term spasm to these motor reactions is quite warranted, as for instance in Jacksonian epilepsy, it is advisable for the present to minimise the possibility of error by confining its use to conditions the result of irritation at any point on a bulbo-spinal reflex arc. Evidently then a tic is not a spasm, pure and simple. For we may suppose the reflex centre shifted from a lower to a higher level, from the bulbo-spinal region to the cortex. The modification effected by the cortex on afferent impressions is at once obvious in altered motor reactions, which appear with the stamp of cortical intervention. To this category belong the tics. If in a given motor phenomenon there is no evidence of actual or previous cortical interference, it is not a tic. If the motor reaction is consecutive to pathological irritation at any point on a bulbo-spinal reflex arc, it is a spasm. If the cortex is or has been involved in its production, it is not a spasm. Should it present, in addition to the fact of cortical participation, certain distinctive pathological features, it is a tic.

These distinctive features have been excellently summarised in an old lecture by Charcot. "However intricate and bizarre may appear the convulsive phenomena known as tics, they are not always as irregular, inco-ordinate, and contradictory, as superficial examination might lead one to believe. On the contrary, they are as a general rule systematised, seeing that in a given case they recur in an identical manner, reproducing and simultaneously exaggerating complex automatic purposive movements that are essentially physiological; they are, in a sense, the caricatures of ordinary acts and gestures. Mere repetition does not, and cannot, evolve a tic in every case. Not all who would may tic."

Such a description suffices to dispel any lingering confusion between tic and spasm, and illustrates the points on which stress is laid in Meige's definition. Tic is a psychomotor disorder, since it is clothed in the form of a convulsion, a perversion of a normal muscular contraction, and consists of a once normal act become illogical, inapposite, absurd. The imperiousness of the impulse and the peculiar satisfaction attendant on submission to it accentuate the importance of the psychical element. Of course it is readily conceivable that a spasm may be the forerunner of a tic, and in many cases no doubt a purely spasmodic reaction may

determine the form and localisation which the latter will adopt; but however difficult it be to retrace the steps taken by the disease in its progress, or to satisfy one's self of the fact of cortical intervention at some stage or other, the rôle played by mental insufficiency in the genesis of tic is fundamental.

There is a danger, it may be, of emphasising the mental at the expense of the physical aspect. Magnan and his school would have it that tic is only one of the manifold expressions of degeneration, "an episodic syndrome of hereditary insanity." This is not very enlightening. Granting that all who exhibit signs of this condition are degenerates, superior or inferior as the case may be, all degenerates do not suffer from tic. Unfortunately the inclination too often is to be satisfied with the designation, and to imagine that therewith discussion terminates. Still more unfortunately, some have altogether lost sight of one of the essential characteristics of the condition, viz., the motor reaction, and have conceived the possibility of its occurrence without any tic at all. Cruchet acknowledges the existence of a "psychical tic," with no external manifestation. Such a paradox needs no refuting.

In view of the ease with which ambiguity arises, the work of analysis must be carried still further.

A tic is not a stereotyped act. It is in this connection that the inadequacy of the term "habit spasm" reveals itself. Guinon holds that tic ought not to be cited in the catalogue of diseases, since ultimately it is nothing more than a deep-rooted "bad habit." There is no call to maintain that all motor bad habits are tics, for a whole host of familiar gestures, tricks and mannerisms do not merit the name, superfluous and even detestable though they be. As long as the movement executed conserves in form the characters of a normal gesture, it is not a tic, but what Séglas calls a stereotyped act. The latter has all the appearance of a normal movement, whereas the former is a "corrupt" muscular contraction, betraying an irresistible imperiousness in its performance and requiring an agonising struggle for its repression. Concentration of the attention may diminish the intensity or even inhibit the occurrence of a tic; inversely, a simple bad habit is manifested preferably during this very concentration. The entire absence of either difficulty or distress in checking the stereotyped act indicates that the subject is psychically sound. To denominate tic as a "habit disease" is accurate enough, and we must expect to find every intermediate variety between the bad habit and the true tic, but this need not deter us from drawing the above-noted distinction.

In this brief development of the theoretical side of the question, it must have been obvious that confusion of thought has been responsible for the violent differences of opinion that characterise recent contributions, yet when we turn to consider the expression of a tic in a motor reaction, we find that here too the investigation of the subject is encircled with perplexities. Not only are the troubles of motility boundless in their diversity, and correspondingly difficult to classify; they bear also so close a resemblance to a whole series of muscular affections that the tendency is to aggregate all and sundry into one great group, under the name myoclonus, and into this chaotic farrago it is to be feared will tumble a crowd of conditions which should be studiously differentiated; tics, electric and fibrillary choreas, paramyoclonus multiplex, &c. Peril lurks in too hasty a generalisation. The scope of myoclonus is at once too inclusive and too exclusive. It may be indispensable; it is certainly not sufficient.

But the possibilities of misapprehension do not end here. On the very nature of the muscular contraction opinion is divided. That a convulsion may be either clonic or tonic is admitted, yet with singular unanimity observers have refused to recognise the existence of such a phenomenon as a "tonic tic," in spite of the instances supplied by clinical examination. So much so that a whole order of facts which, in derivation, essence, and external features, ought to be identified with the tics has been passed over in silence. Cruchet thinks that to extend the term tic to tonic contractions, such as mental torticollis, mental trismus, or permanent blepharospasm, is entirely to outstep the limits of its application. Oppenheim believes that the restriction of convulsive tic to clonic convulsions is not only warranted, but simplifies and elucidates the whole question.

To this view we conscientiously demur. The primary meaning of the word tic is not strained by applying it to a contraction of a certain duration; there is, on the contrary, historical justification for so doing. It is owing to this widening of the horizon of a tic—a proceeding strongly advocated by Brissaud and his pupils—that fresh light has been thrown on torticollis and kindred states. The interesting topic of the relations between torticollistic and torticollis-spasm is one which cannot be entered on in this place, but enough has been said to indicate the lines along which advance is likely to be made. In a word, recourse to the epithet convulsive is superfluous, and tic is to be taken as signifying either a clonic or a tonic contraction. The gain in conciseness is not neutralised by any loss of precision.

It has seemed fitting thus to elaborate the analytic aspect of the subject, for one cannot but be struck with the urgency of a rigorous schematisation. As it is, diagnosis will remain a matter of some complexity until the labour of analysis and synthesis alike is perfected. Many problems await solution, but that is no reason for continuing ignorant of the results already attained. It will not do to neglect the tics. A tic does not constitute a menace to life, yet the more it is repeated the more inveterate it becomes, and the greater its tendency to become generalised, while its indefinite prolongation, its association with grave mental symptoms, and its occasional termination in dementia, are excuse enough for eyeing its first premonitory exhibition with mistrust and combating it with vigour. Within recent years excellent therapeutic progress has been made by the method of re-education, and by psychomotor discipline, so that there is no need for the physician to consider himself helpless in presence of a tic, and the fact that the outlook is good is an additional plea for accuracy of diagnosis. A distinction between facial tic and facial spasm can by no means always be readily made, yet the treatment of the two is not identical. It is not at all an uncommon occurrence for chorea to degenerate into tic, and recognition of this truth is of importance, since treatment calculated to cure the one will only serve to accentuate the other. It is satisfactory to note that attention has been directed to this point in a recent lecture by Still.[1] For detailed accounts of therapeutic methods, as for the discussion of many parts of the question impracticable in a summary, reference must be made to the authorities cited, and to Meige and Feindel's book on "Les Tics et leur Traitement," a review of which has already appeared in BRAIN.[2]

S. A. K. WILSON.

[1] *Lancet*, December 16, 1905, p. 1,754.
[2] BRAIN, 1903, Vol. xxvi., p. 462.

Paralysis and other Diseases of the Nervous System in Childhood and Early Life. By JAMES TAYLOR, M.A., M.D., F.R.C.P., Physician for Out-patients to the National Hospital for the Paralysed and Epileptic, Queen Square; Physician to the North-Eastern Hospital for Children, and to the Moorfields Eye Hospital. London: J. and A. Churchill, 7, Great Marlborough Street, 1905.

Treatise on the Nervous Diseases of Children, for Physicians and Students. By B. SACHS, M.D., Alienist and Neurologist to Bellevue Hospital, New York. Second Edition, Revised. New York: William Wood and Company, 1905.

DR. TAYLOR is to be congratulated upon his recently published work on "Paralysis and other Diseases of the Nervous System in Childhood and Early Life." A treatise specially devoted to nervous disease in early life was a distinct desideratum, for although most writers on diseases of children deal to some extent with these disorders, it is hardly practicable to deal so fully with them in a general text-book as Dr. Taylor has been able to do here; and although in America Dr. Sachs has written on the subject, it has not, as far as we know, been treated specially by any English writer before. The title of Dr. Taylor's work disarms criticism so far as the subject matter is concerned, for he does not limit the scope of his work to nervous disease in children, he includes many diseases which are never, or hardly ever, seen in childhood, such as electrical chorea, Huntington's chorea, hereditary tabes dorsalis, and hereditary optic atrophy. Curiously enough, while many excessively rare conditions are described, there is no mention of such a peculiarly infantile disorder as spasmus nutans, which, compared with the diseases just mentioned, is almost a common affection. But more curious perhaps is the devoting of a chapter to achondroplasia in a work on nervous diseases; but here, as in other places, for instance, where some pages are occupied with a description of congenital dislocation of the hip and its diagnosis from coxa vara, the explanation evidently is that the author has in his mind the problems of diagnosis as they arise in actual practice; achondroplasia is apt to be mistaken for cretinism, coxa vara for congenital dislocation of the hip, and both these for pseudohypertrophic muscular paralysis; so that the anomaly of subjects is less than at first appears, and in reality the value of Dr. Taylor's book is enhanced by this practical view of his subject.

Dr. Sach's work is upon somewhat different lines; it is a general text-book of nervous diseases with some special reference to children: diseases such as exophthalmic goitre, tumours of the spinal cord, and disseminate sclerosis are described in detail; and many other conditions which though usually seen in the adult are occasionally seen in childhood, are discussed at full length, in some instances at much fuller length than diseases almost peculiar to children. It is noteworthy that disseminate sclerosis is stated by Sachs to be "distinctly a disease of early life," and he quotes Totzke as recording six cases under the age of 2 years, and several between 4 and 14 years of age; he mentions only one case, which began at 10 years from his own observation, and in this there was apparently no *post-mortem* verification. One may suspect that the ataxia which sometimes follows specific fevers, and which has been shown to be due to an inflammation affecting especially the cortex of the cerebellum, has sometimes been mistaken for disseminate sclerosis, and in congenital cases, such as some of those described by Totzke, which probably correspond with the condition described by Batten as congenital ataxia, there is at least a likelihood that developmental faults quite distinct from the pathological changes of disseminate sclerosis account for the symptoms.

Posterior basic meningitis is described by Dr. Taylor entirely apart from epidemic cerebro-spinal meningitis; the possibility of these being respectively sporadic and epidemic manifestations of one and the same meningeal infection is not considered. Various writers, however, including Osler, Koplik, and Sachs, have recently favoured this view, and there can be little doubt that many of the cases described as cerebro-spinal meningitis in America would be called posterior basic meningitis in England. In the use of lumbar puncture as a therapeutic method in meningitis, the author's experience agrees with that of many other observers; he says it is of no curative value in tubercular meningitis, but both here and in suppurative meningitis it may ameliorate symptoms. In the recent epidemic of cerebro-spinal meningitis in New York, it has been practised extensively, but Huber writing with reference to children says the results have been disappointing from a therapeutic point of view. Heubner, in Berlin, however, says that pain was relieved by removal of 20 to 40 c.cm. of fluid, and that many observers thought that they had obtained recovery by repeated use of lumbar puncture in these epidemic cases.

In Dr. Taylor's description of the cerebral palsies the patho-

logy and etiology is very fully considered, and it is interesting to note how largely views have been modified as to the pathology of infantile hemiplegia within the past few years. Although in Sachs' work the polioencephalitis cortica'is acuta of Strümpell is not accepted without question, and in the category of pathological conditions causing cerebral palsy in children, figures only as a suggestion at the bottom of the list, in Dr. Taylor's work the majority of cases of infantile hemiplegia are stated to be the result of an acute encephalitis, which he regards as analogous to acute anterior poliomyelitis and not improbably identical with it in its cause. Meningeal hæmorrhage, to which most writers, including Dr. Sachs, have attached much importance, is given the last place by Dr. Taylor. The view that acute anterior poliomyelitis and these cases of encephalitis are due to one and the same pathological process, raises certain difficulties; for, as this author himself points out, the spinal cord lesion is probably the result of a special and peculiar poison, and occurs occasionally in epidemic distribution; he points out also the very striking seasonal incidence of acute anterior poliomyelitis. If the two conditions, infantile hemiplegia and acute anterior poliomyelitis, be the result of the same poison whatever it may be, there should be a close correspondence in their seasonal variation, but he mentions no special seasonal incidence in the onset of infantile hemiplegia, nor so far as we are aware, has any such special incidence been recorded in that affection. Moreover, when epidemics of acute anterior poliomyelitis have occurred, there has been no special prevalence of acute encephalitis, so far as we know; Dr. Taylor, however, refers to one suggestive case, presumably that recorded by Mœbius, in which one of two children in a family developed the spinal cord affection, and the other the cerebral at the same time. He states that in "about one-third" of all cases of infantile hemiplegia the disease appears in the course of an attack of one of the specific fevers; this experience would seem to be quite exceptional. Wallenberg found 40 out of 160 to follow infectious diseases, and Osler found only 16 out of 120 to have begun in connection with, or just after, a specific fever; but the latter figures certainly, and probably Wallenberg's also, include whooping-cough, and according to Holt infantile hemiplegia occurs much more frequently with pertussis than with any of the other specific fevers. The connection with whooping-cough may be, and is, in many cases, very different from the relation of hemiplegia to other specific fevers, it is merely the result of mechanical strain rupturing vessels in the

meninges or brain; moreover, even in the other fevers there are often obvious causes for the occurrence of hemiplegia, quite apart from any primary infective encephalitis. Dr. Taylor refers to embolism from endocarditis in scarlet fever, and to thrombosis with marasmus; there is also a well-known tendency to thrombosis in typhoid, and the degeneration of the myocardium which occurs in diphtheria and in other specific fevers is known to cause thrombosis and embolism; until the part played by such causes in the association of hemiplegia with specific fevers can be fairly estimated, it is difficult to judge how far the theory of a primary infective encephalitis receives support from the association with the specific fevers.

In the etiology of cerebral diplegia, illness of the mother during pregnancy is mentioned as a factor of definite etiological importance; alcoholism, however, is not considered in this connection. It seems at least likely that it plays some part, whether it be present in the mother or the father; in the production of idiocy it is generally admitted to be one factor; 19·5 per cent. of the cases of idiocy at Darenth Asylum showed parental alcoholism; Koenig in a recent comparison of the etiology of cerebral palsies in children with that of idiocy showed that while 15 per cent. of cases of idiocy showed strong alcoholism in the father, no less than 23 per cent. of cases of cerebral palsy gave a similar history. The same writer regards "psychic trauma," mental shock or emotion in the mother during pregnancy, as a factor, and gives statistics showing the presence of this factor in 23 per cent. of the mothers of children with cerebral palsy.

Amaurotic family idiocy is classed by Dr. Taylor as a form of cerebral diplegia on the ground that the degeneration of nerve cells differs in extent, but not in kind, from that found in other forms of cerebral diplegia; its gradual development after birth is referred to some congenital lack of vitality in the cells, the condition to which Gowers has given the name abiotrophy. It is stated that no case has been reported in any but children of Jewish race; quite recently, however, a case has been recorded by McKee, of amaurotic family idiocy in a Gentile boy, and a careful histological examination showed generalised degeneration of nerve cells throughout the nervous system as found in other cases.

The suggestion put forward by Hirsch, and also by Russell and Kingdon, that the disease is due to some toxin acting through the mother's milk has been declared untenable by Sachs; he quotes, as an instance favouring this view, the case of a Jewish family in which the first child fed on sterilised milk was healthy,

the second and third children were both breast fed, and one certainly, and probably the other also, died of this disease; but on the other hand he says that several of his cases had never been nursed by the mother, and yet had developed the disease. Sachs agrees with Taylor in accepting abiotrophy as the determining cause of the cell degeneration which is the chief feature of the disease, and he, too, notes the close resemblance between the lesions in some cases of spastic diplegia and those of amaurotic family idiocy.

Chorea is described very fully in Dr. Taylor's work, and this author inclines to the view that this disease is in the large majority of cases the result of an infective process, but that the nature of the infection is perhaps not always the same. He attaches little importance to the lesions, cortical cell changes, perivascular infiltration, capillary embolisms, &c., which have been recorded by many observers, they are to be regarded as the result of complications; the cause of the irregular movements is rather to be sought in some functional disorder of the nerve-cell itself. The recent bacteriological findings, the presence of diplococci about the small vessels of the cortex, may explain the instability of nerve-cells either by direct action of the bacteria or by the action of some bacterial tòxin.

The bearing of canine chorea upon the relationship of this disease to rheumatism is not considered; the affection in dogs is said to be definitely related to distemper, which no one apparently supposes to be rheumatic; but it has yet to be proved that the so-called canine chorea corresponds to the chorea of childhood. It is stated that chorea is perhaps never met with in children under the age of 3 years; undoubtedly it is exceedingly rare under that age, but we have seen and recorded a case with articular rheumatism, endocarditis and chorea at 2 years and 10 months. To the excellent account of the treatment might be added the use of ergot, which has recently been advocated by Dr. Eustace Smith.

A chapter is devoted to stammering, which is made synonymous with stuttering; and here we confess to much sympathy with German writers, Gutzmann and others, who have drawn a sharp distinction between stuttering and stammering. For it does seem altogether incongruous to describe idioglossia and lisping as varieties of the same affection which is seen in such spasmodic co-ordination neuroses as aphthongia and the violent efforts at articulation of which Kussmaul's description is given.

In the chapter on night-terrors no mention is made of the

occurrence of day-terrors, the Pavor Diurnus of Henoch, but, indeed, they are rare, so that their omission is of no great importance.

In discussing the pathology of infantile paralysis, Dr. Taylor, whilst agreeing with the observations of Dr. F. E. Batten as to the prominence of thrombosis in the morbid anatomy of acute anterior poliomyelitis, differs from that observer, and also from Dr. Sachs, in regarding this thrombosis as probably the result of a special and peculiar poison. No opinion is expressed as to whether the thrombosis is the primary change as Dr. Batten contends, or whether some inflammation occurs first with secondary thrombosis, as Drs. Head and Campbell have argued.

The theory that the disease may be dependent upon a primary affection of anterior horn-cells, with secondary changes in the interstitial tissue, is dismissed as an untenable view based upon observations taken at too late a stage of the disease to be of any value in the interpretation of its initial changes. Dr. Batten, however, whose careful observations on this disease entitle his opinion to much weight, holds that there are cases in which the primary affection is in the anterior horn cells, and that such cases form a clinical group having symptoms differing in certain well-defined respects from the commoner type of acute anterior poliomyelitis.

Dr. Taylor's work, as he himself points out, is an expression of personal opinion on subjects which have interested him; it does not claim to be an exhaustive text-book, even of the special department of disease with which it deals. Whilst, therefore, the absence of several nervous affections of childhood which one might naturally expect to find described in such a book is to be regretted, we recognise that what is lost in completeness is gained in attractiveness, for what is written *con amore*, and from personal observation, is ever more interesting than the omniscient dulness of the routine text-book. Laudatory comment is unneeded for a work such as Dr. Taylor's; "good wine needs no bush"; suffice it to say that there can be no doubt that so valuable a contribution to the subject will take a high place amongst the standard works on diseases of childhood and early life.

G. F. Still.

Physiologische und Klinische Untersuchungen über das Gehirn. By EDUARD HITZIG. Berlin, 1904. (Hirschwald.)

"CONQUERED not by my opponents, but by all-powerful fate, which has almost entirely robbed me of my eyesight, now and for ever I lay down the knife, the pen, and the sword." These words in Professor Hitzig's preface will be read with the deepest sorrow by all neurologists. But a little while since, as Hughlings Jackson lecturer, he gained the highest honour it is in the power of the Neurological Society of Great Britain to bestow. For more than thirty years his name and his work have inspired deep respect among physiologists, and, long though his activity has lasted, his concluding works leave us with the feeling that but for this misfortune much more would have been accomplished.

The book is divided into two portions; the first contains a collection of all his earlier contributions, and these are not bare reprints, each paper is enriched by annotations and considerations of researches which have since been published by others. On re-perusing these interesting *brochures*, arranged in serial form, our admiration is immediately secured by observing how methodically Hitzig planned and set about his life's work, what pains he took first to lay down sound foundations, whereon to build up consecutive works all dependent on one another, all in regular order, and all complete. The discovery, made in the year 1870, that the surface of the brain of the dog is susceptible in places to electrical excitation, was alone sufficient to make the name of Hitzig famous. Not satisfied, however, with the results bearing on the localisation of function obtained by this means, he proceeded to supply deficiencies with a brilliant series of extirpation experiments. Next he succeeded in locating the motor area in the ape, and finally enjoyed the distinction of being the first to publish an observation on the effects of a localised lesion in man.

Many of these early papers are devoted to the localisation of the motor area, and in view of the controversies which have arisen on this subject, it is instructive to find Hitzig first stating emphatically that all the motor centres lie in the anterior central convolution, and then supplying details which agree, not absolutely but remarkably well, with those yielded by the most recent investigations. And when we consider that these observations were made when electricity had been employed for physiological purposes by this man alone, when histology had not been exploited as an adjuvant, and when apes were so scarce that one

only could be procured for experiment, we see a register of the high standard of this master's work. Indeed, among pioneers in experimental neurology, there is none who has established more principles of brain physiology, none who has had less to take back as incorrect, and although he has indulged in polemics more than others, his opponents must concede that he has always met them with fair weapons.

The second half of the book consists of matter which has appeared more recently in the *Archiv für Psychiatrie und Nervenkrankheiten*. It is entirely devoted to the visual sense, and is the product of a great number of experiments on the dog, which are recorded in detail and faithfully illustrated. First, the effects of lesions of the occipital lobe on movement are discussed. In such cases Hitzig has frequently seen what he calls *Defecte der Willensenergie*, and originally thought that they denoted loss of motor impulses issuing from the destroyed parts; but now he recognises the inconstancy of the disability, and abandons it as inexplicable. Attention is next drawn to the production of visual changes by destruction of cortex away from the occipital lobe. Hitzig is assured that transitory hemiopic defects follow operations on the cortex and white substance of the sigmoid gyrus of the dog—that is, the motor area. This result has no parallel, so far as I am aware, in the cases of the human being and higher ape, and again the Professor is unable to supply a satisfactory explanation. Another interesting result was that when the temporary hemianopia caused by a lesion of the sigmoid gyrus had passed off, a lesion in the occipital region of the same side did not intensify the visual disturbance. Further, it was frequently observed that the left hemianopia to be expected from a lesion of the right occipital lobe did not occur if, previously, by lesion of the left occipital lobe, a right hemianopia had been produced. It appears correct to explain these effects by assuming that the dog is an animal in which sight is strongly represented in the primary subcortical centres.

In this part of the book Munk's conclusions are criticised with great severity. According to Hitzig partial destruction of the occipital lobe of the dog produces no permanent change in particular, the partial permanent cortical blindness of Munk does not occur. Also, the projection of the retina on the occipital lobe, as Munk describes it, is disputed; it is only admitted that a temporary quadrantic hemianopia downwards attends lesions of the anterior half of the visual area and an upward hemianopia lesions of the posterior portion. And, in Hitzig's experience,

lesions of Munk's zone A produce no psychic blindness, but only transient crossed hemianopia, hence the psychic blindness of Munk must be quite different from that which has been recognised in man, and must arise from simple amblyopia.

Hitzig brings forward such a fund of experimental data in support of his different arguments that he almost places himself outside the bounds of criticism, and yet, since the visual cortex has been recently submitted to thorough investigation by the microscopist, we cannot refrain from looking at these questions from the histological standpoint, and the regret forces itself upon us that this magnificent series of experiments was performed before the area striata—so easily demonstrable in the dog—and the homologies of the visual area were determined. If the area striata represents the "visuo-sensory" area, as appears certain, and if "visuo-sensory" cortex is invested by "visuo-psychic" cortex, as appears likely, surely these points in anatomy will need most careful attention, before experiments made to instruct us regarding hemianopia, partial or complete, the restitution of vision, psychic blindness, and so on, can be freed from misinterpretation and confusing imperfections.

ALFRED W. CAMPBELL.

The Diseases of Society and Degeneracy. By G. FRANK LYDSTON, M.D. J. B. Lippincott Company, Philadelphia and London, 1904, pp. 626. Price 15s. net.

THOUGH the views in this book have been promulgated by an author who has lived for a considerable time in Chicago, and for a time as resident surgeon to the Blackwell's Island Penitentiary, New York, yet a considerable amount of it will apply equally to criminology in England. The author states that "this work, then, is not a treatise on sociology, criminology, criminal anthropology, penology, nor yet upon that latest omnibus to which some assign all moral or psychic aberrations—degeneracy, but is intended to comprehend all of these subjects, in so far as they bear upon social disease in its various divergations." From this it will be seen that the author has not limited himself to any one particular study, but has treated of a great number. The census of 1890 showed that criminals, paupers, and insane, numbered about

250,000. Approximately one person in every 320 in the United States is a criminal, insane, or a pauper. With regard to heredity, which the author says is of especial potency in the evolution of crime, he quotes the statistics of Professor Poellmann, of the University of Bonn, who investigated the lives and characters of the descendants of a woman who was a confirmed drunkard. She was the direct progenitor of 834 persons, and the total cost to the State of caring for the paupers and punishing the criminals amounted to 1,206,000 dollars. The history of the "Juke family" is another case in point. The author divides criminals into four types: (1) instinctive criminals, born criminals, of which the moral imbeciles and morally insane are types; (2) criminals by impulse; (3) epileptic and insane criminals; and (4) political criminals. He refers to the efforts of Moreau, of Tours, who endeavoured to formulate the biologic effects of degenerate heredity, and himself enumerates twenty special cases of social disease. He also refers to suggestion as a cause of crime, and very rightly refers to the power of the press. The reviewer has for many years been of opinion that the publication of the morbid details of the lives of criminals in prisons causes mentally weak persons to become criminals themselves, and he is glad to find that in this opinion he is supported by Dr. Lydston. The importance of the fore-brain is admitted by the author, who expatiates on insanity in its relation to crime, the necessity for laboratory study of defectives, and the fact that suicide is more intimately associated with insanity than is any other anti-social act. Alcoholism is a common cause of crime, and lying and deceit are second nature to those addicted to the narcotic habit; but it is satisfactory to know that one of the most important factors of the prophylaxis of insanity is physical training. A chapter is devoted to anarchy in its relations to crime, and the author shows that John Wilkes Booth, Charles J. Guiteau, Garfield's assassin, and Czolgosz, the murderer of President McKinley, were all insane, and actuated by insane impulses. Sexual vice and crime occupy two chapters, and the author is very outspoken on the causes which produce prostitution. His chapter on the treatment of this sexual vice and crime contains many sensible remarks: that boys should be taught that physical perfection and early sexual indulgence are incompatible, and that "youth should be taught that to control one's appetite makes a man a king among men, but that allowing his appetites to control him makes him a slave," are not only true, but should be taught the boy by his parent or guardian. Many boys go wrong through innocence, and a

masturbator should be looked upon as a curse to a school. The boy whose muscles are daily properly trained, and who takes an interest in games, is much less likely to go wrong than the loafer who has no healthy pursuits. Young girls should also be given to understand that spinsterhood is no disgrace, and far preferable to an unhappy marriage. The chapters on genius and degeneracy and physical and psychic characteristics of the criminal are well worth reading, but the review of this book has already exceeded its limit. There are numerous illustrations in it, which add much to its interest, and we can only hope that it will be read, as it should be, by all social workers.

FLETCHER BEACH.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF THE UNITED KINGDOM.

At the Clinical Meeting held at 11, Chandos Street, Cavendish Square, on Thursday, October 26, at 8.30 p.m. (patients in the rooms at 8 p.m.), the following cases were shown:—

Dr. H. G. Turney.—*A case of generalised spasm, most marked in the muscles of the back, probably due to a tumour in the neighbourhood of third ventricle.*

[34] The patient is a boy, aged 16. The family history is negative; both parents are alive and well, and his one brother is a normal athletic youth. The patient's previous history is equally blank, save for childish ailments. His present condition has been coming on for about six months. Onset was vague, but less than a year ago he was bicycling and was considered to be in perfect health. He has always been a very reserved lad, but up to the average in mental development, and his mother maintains that his illness has not altered him mentally. There has been no headache or vomiting and no pain of any sort throughout.

On examination.—Patient is well grown, but emaciated. His movements are slow and difficult. The arms have a tendency to remain without support in any position in which they have been placed. The spine shows an exaggeration of the lumbar concavity and is held rigid, the back, when he stands, forming an angle of about 50° with the thighs. In the cervical region some movement is possible, but it is very limited, and the head can be turned only slightly from side to side. The stiffness of the back disappears under an anæsthetic, and an X-ray examination proved negative. The lower limbs are stiff, the legs being held at an angle with the thighs. Patient can stand with the eyes shut and can walk, though slowly, and with the limbs in the positions just described. There is optic neuritis in an early stage. No actual paralysis can be made out, and there are no changes in the electrical reactions. The deep reflexes are much increased, with ankle clonus and the

Babinski sign. There is loss of control over the bladder, the bed being constantly wet. Sensation is unaffected.

Dr. ERNEST JONES.—*Multiple bilateral contractures simulating pseudo-hypertrophic muscular paralysis. (An aberrant form of the Nageotte-Wilbonchewitch syndrome.)*

[35] F. L., male, aged 9½, out-patient under care of Dr. G. F. Still.

Family history.—Has one healthy younger sister, and no brother; none dead. Mother has had four miscarriages. Mother has three sisters and one brother well. Two sisters died in childhood. Father has seven brothers and one sister well; none dead. No similar condition to that of patient known in family.

Personal history.—Walked at 2, but never steadily. Gets pain in thighs when tired. Two years ago, when starting physical drills, it was noticed that he could not elevate his arms. Hand movements have always been clumsy. The troubles do not seem to be progressive.

Present condition.—General. Aspect unusual, owing to cheeks being very full and red, and face puffy. Chest emphysematous. Short for age. Mentally bright. Cranial nerves and fundus normal. Reflexes, sensation and sphincters natural. Muscles are everywhere weak and poorly developed, save for following exceptions:—

Posture and gait.—He stands with flexed hips and knees, and there is compensatory lordosis. This all disappears at once when he lies down. He walks with a waddling gait, limping on the right side; the joint flexion is most marked on this side. The boy gets up from the supine position in a normal manner.

Upper extremities.—(*a*) Shoulders. At the shoulder joint there is limitation both passive and active of abduction, and to a less extent of flexion and external rotation; the arm cannot be raised much above the horizontal. The scapulæ are placed further from the middle line than normal, but are not winged; the lower angles are displaced more outwards than the upper; the scapulæ move a little earlier than they should when the arm is raised, but not when the arm is lowered. The deltoids, rhomboids, lower part of trapezius and serrati magni are overdeveloped, are harder than normal. The latissimus dorsi and teres muscles are contracted on either side, especially on the right, and are of denser consistence than normal. There is no muscle atrophy either of the pectoral or other muscles.

Skiagrams show no definite joint changes.

(*b*) *Hands.*—The interphalangeal joints cannot be fully extended.

This is so in every finger and thumb, but is most marked in the terminal joints of the third and fourth fingers; the limitation is unaffected by the position of the wrists. The terminal phalanges of the fourth fingers feel thickened. Skiagrams show distinct condensation of all the terminal phalanges, and broadening, with only slight condensation of the other phalanges, so that they are bulged in the middle and not "waisted" like the metacarpals. The wrists are swollen, especially the left, where the synovial sac is felt to be large; there is undue laxity of these joints, especially of the left, which allows marked lateral mobility.

The grasp is weak, and is not strengthened by fixing the wrists. This weakness is partly, but not altogether, accounted for by limitation of flexion of the fingers, so that the hand cannot be closed even approximately. On separating the fingers, hyperextension of the metacarpo-phalangeal joints takes place; this is unaffected by the fixation or position of the wrists. Besides the interossei, the other hand muscles act fairly well.

Lower extremities.—There is slight limitation of extension and abduction; in the latter movement the abductors get tight earlier than is natural. The calf muscles are perhaps a little hard.

The skiagrams show that the head of the left femur is only ossified for a very short distance above the epiphysis. The right hip joint shows only slight defect. The acetabula are badly formed, but the cervical angles are normal. Ossification is already present in the lesser trochanters.

Dr. Colin K. Russel.—*Case of juvenile type of general paralysis of the insane.*

[36] G. B., aged 20, labourer, single, admitted under Dr. James Taylor, September 4, 1905.

Past History.—Eight months' child, always bright and active at school.

Family History.—Father had lues, and died of diabetes and tuberculosis. Mother alive and well; of her first four pregnancies three were born dead and one miscarried. The eldest living child suffers from keratitis, patient is the second.

Past Indications.—Since age of 16 he has become apathetic, with slurring and indistinct speech, cannot fix his attention, and has lost his memory. Three months ago transient palsy of right arm, with aphasia.

Present Condition.—Pupils equal, active to light and accommodation. Marked tremor about eyes, mouth and in tongue. Reflexes brisk.

Dr. F. E. Batten.—(*a*) *Ulnar neuritis, with fusiform enlargment of the nerve, occurring fifteen years after injury to the elbow.*

[37] R. S., aged 32. Eighteen years ago had a severe cog-wheel accident, with injury to the left elbow joint.

Three years ago the patient noticed numbness of the left hand, and about the same time wasting of the muscles.

At the present time there is weakness of the left hand, with atrophy of the interossei and adductor pollicis muscles. "Protopathic" sensation only is present over the distribution of the ulnar nerve. Localisation is defective, extremes of heat and cold can only be distinguished, and touch produces the sensation of "pins and needles." There is a fusiform enlargement of the ulnar nerve as it passes over the internal condyle.

(*b*) *Defect in upward and downward movement of the eyes. Mental impairment.*

[38] T. C., aged 60. Was quite well until June 18, 1905. Went to bed well, but in the morning was found in a drowsy condition. His wife got him up and he went down stairs, but he seemed to get worse, and he was put to bed, and for the next three weeks was said to be paralysed all over. There was no headache, no vomiting, and no loss of consciousness, but his speech was defective. He gradually recovered, and was able to get about in three weeks, but his memory has always been defective since. He cannot even remember where he lives. He knows his name, and can say it indistinctly. Little or no improvement has taken place in the last few months.

His face suggests paralysis agitans, and is wanting in emotional expression. He can, however, perform all movements of the face well. The movements of the head and eyes to the right and left are normally performed. The movement of the eyes upward is defective, and on attempting this movement the lids are raised, and leave a considerable interval of sclerotic above the cornea. Downward movement of the eyes is also very defective, but if the patient is first made to converge, then the downward movement of the eyes is relatively good.

The pupils are equal and react to light and on accommodation. There is no word-deafness, no word-blindness, and no limitation of the fields of vision. Knee-jerks, active. Plantars, flexor.

Dr. Farquhar Buzzard.—*A boy with some cranial nerve palsies.*

[39] W. D., aged 8.

Family and previous history good.

Present illness has an indefinite onset. For one year general listlessness and fatigue; six months getting thin, and eyes not closed during sleep; four months difficulty in swallowing; two

months defective movements of eyes; one month articulation affected. No pain, headache, vomiting, or sphincter trouble.

Present condition.—Nervous and uncommunicative. General nutrition improved since admission. Taste, smell, and vision normal. Optic discs healthy. Pupils react well. Weakness of both external recti, left more than right. Slight ptosis, left more than right. Both motor and sensory functions of the fifth nerve unaffected. Marked weakness, wasting, and tremor of both sides of face, left more than right. Bilateral abductor paralysis of the larynx. Hearing good. Palatal movements deficient, but not absent. Tongue wasted, feeble, and tremulous. Swallowing slow and difficult. Limbs and trunk normal. Reflexes of the normal character.

Dr. LEONARD GUTHRIE.—*Two cases of (?) early Friedreich's disease.*

[40] (*a*) Boy, aged 4. Born healthy, except that the eyes were at first turned up, gradually assuming normal position. Has been noticed, however, to bend head on looking at objects straight in front of him, as though fixing them with the lower half of the retina.

Began to walk at $2\frac{1}{6}$ years, but has never walked well. Seemed to be giddy, and would sometimes stagger and fall. He is a well-made, healthy-looking child, mentally backward, but not markedly deficient.

Pupils and fundi are normal. Lateral nystagmus present, and most marked on extreme deviation.

Speech babyish, drops initial consonants of words, but can repeat them correctly by imitation.

Can walk alone, but unsteadily, on wide base (there is, however, some genu valgum). Unsteadiness is much more apparent, and Rombergism is present on getting up after rest in bed.

Upper extremities.—Not ataxic. Muscles not wasted nor hypertrophied. Muscular power good, but moderate hypotonia present.

Feet considerably arched, but condition does not amount to pes cavus. No scoliosis nor kyphosis.

Sensation nowhere impaired.

Sphincters—Nocturnal enuresis is common, but can control sphincters by day, though micturition is frequent.

Reflexes.—Knee-jerks and Achilles jerks are absent. Plantar response active, but indeterminate, sometimes flexor, sometimes extensor in type. Arm tendon-jerks not obtained. Abdominal and cremasteric reflexes brisk.

Family History.—Phthisis on father's side. Mother had serious attack of pneumonia when five months pregnant, and was hardly convalescent when patient was born.

A first cousin (paternal), a girl, aged 14, did not walk until past 3 years old, and has always been unsteady and apt to stumble and fall. There is some spastic inco-ordination of the right leg. The knee-jerks are exaggerated, ankle clonus absent. No deformity of feet, but slight scoliosis present. Eyes, speech, sensation, and sphincters normal. She is dull mentally, has a large (?) hydrocephalic head, and undersized body.

[41] (*b*) Boy, aged 11½. Healthy when born. Has always been weak on his legs and unsteady in walking.

Eighteen months ago fell off van and sustained "slight fracture of the skull with concussion of brain." Recovered entirely in a month, but weakness of the legs was as before, and during the last year has increased.

Patient is a delicate-looking anæmic boy. Intelligence good. Speech unaffected. Pupils and fundi normal. Slight nystagmus at times on lateral deviation. Muscular development fair, but slight winging of scapulæ, especially the left. No scoliosis nor deformity of feet. Slight ataxy of upper extremities. On approximating forefingers from a distance, misses contact by about an inch. Gait not ataxic, but has difficulty in walking 8-inch path. (This has improved after practice.)

Slight Rombergism present.

Knee-jerks and Achilles jerks absent. Arm-jerks and plantar reflexes unobtained. Sensation unimpaired. Muscular sense unaffected. Sphincter action normal.

Family History.—Unimportant.

Dr. COLLIER.—*A case of acute encephalitis resulting in partial left hemiplegia, and complete loss of vision. Optic discs healthy. Pupil reactions normal.*

[42] A child, aged 2½ years, was suddenly seized with head retraction and left hemiplegia without loss of consciousness. During the following week she had three attacks of general convulsions, most severe in the region of the face. She did not regain consciousness after the last of these attacks, but lay in an unconscious state with marked head retraction for five weeks, after which time she speedily regained consciousness and intelligence. The hemiplegia slowly improved, and eight months later she could stand, walk and use the arm a little. She has been absolutely blind ever since regaining consciousness, eight months ago. The optic discs are quite healthy, and the pupils react normally. It is suggested that the visual loss is owing to destruction of the calcarine cortex of both hemispheres.

ABSTRACT of a Paper upon "Some Investigations on Acute Rheumatic Nervous Affections," by Dr. POYNTON and Dr. ALEXANDER PAINE, read at 11, Chandos Street, Cavendish Square, on Thursday, November 23, at 8.30 p.m.

The authors, as a wish had been expressed that the entire question of the etiology of rheumatism should be open to discussion, devoted the commencement of the paper to this point. After repeating their claim that they had proved that a diplococcus was a cause of acute rheumatism, they discussed the various objections to its acceptance, and criticised their critics. They asked that the members of the Society would for the moment, at any rate, accept the view that this diplococcus was a cause of acute rheumatism, for it was the basis of the argument by which they hoped to explain the investigations they had been making upon the pathology of chorea. These investigations had commenced six years previously, and in May, 1901, in the *Lancet*, they had elaborated in some detail the view that rheumatic chorea was a result of the diplococcus infection. Granted that the diplococcus was a cause of rheumatic fever it was essential to produce evidence of its presence in the nervous system or general circulation in rheumatic chorea, at a time when the rheumatism was active, and had been the cause of death. Dana in 1894, and Apert in 1898, had found a diplococcus under these conditions, then in 1899 Westphal, Wassermann and Malkoff, isolated a diplococcus from the cerebrospinal fluid in a fatal case of pericarditis and chorea, and produced arthritis in eighty rabbits. In 1900 the authors produced choreiform movements in a rabbit with their diplococcus, and in 1901 verified the occurrence of the diplococcus in the cerebrospinal fluid in fatal rheumatism with chorea. In 1903 Beaton and Ainley Walker succeeded in isolating a diplococcus from the blood in the heart, and from the urine *ante mortem*, in three cases of chorea, and also obtained experimental results in rabbits. The authors again, at the International Congress in 1903, recorded the same experience. The experimental results included not only arthritis, but also the production of endocarditis and pericarditis.

Choreiform movements in rabbits had been observed independently by Meyer in 1902, and by Beattie with a diplococcus isolated from rheumatic arthritis in 1904.

In the present communication two further cases were recorded in which the authors had succeeded in isolating a diplococcus from the cerebrospinal fluid of children dead of fatal rheumatism with chorea. In both these cases they had advanced a step

further by demonstrating the diplococci in the pia mater, thus confirming their suggestion in 1901 that this membrane would be the most likely spot in which to find them, and that the most probable localities would be in the neighbourhood of the minute blood capillaries. This view had been based upon the discovery of the diplococci in that situation in the rabbit that had developed twitching movements.

In one of these two cases they had not only succeeded in demonstrating the diplococcus in the pia mater and in isolating it from the cerebrospinal fluid, but they had also succeeded in producing on intravenous inoculations, arthritis, endocarditis and pericarditis, in a rabbit.

For this case they had been indebted to Dr. B. Lees. The patient was a boy of rheumatic parentage, aged 9, who was admitted to St. Mary's Hospital in a second attack of rheumatic fever. The symptoms had been first tonsillitis and then multiple arthritis and general chorea, finally fatal pericarditis.

The cultures from the pericardial fluid, blood and cerebrospinal fluid, had all shown the presence of the diplococcus. The morbid anatomy of chorea, they admitted, still required further investigation. A difficult point to decide was as to whether chorea was the result of a general rheumatic toxæmia, or of multiple minute local lesions. They inclined to the latter view, and compared it with the embolic theory elaborated by Hughlings Jackson. From this it differed in detail in that it seemed probable that the diplococci escaped out of the blood capillaries and produced lesions external to them. In the acute stage there resulted thrombosis, minute hæmorrhages or perivascular exudation, in the late stage of the chronic cases perivascular fibrosis. The toxins produced locally would probably cause fatty change in the nerve-cells, chorea would thus be a mild form of meningo-encephalitis and possibly meningo-myelitis. This view of the morbid anatomy was supported by the results of Reichart. The extent of their own investigations could be tabulated thus :—

(1) They had isolated and cultivated the diplococcus from the cerebrospinal fluid in four cases of fatal rheumatism, in three of which there had been chorea at the time of death.

(2) They had produced twitching movements, arthritis, endocarditis, and pericarditis by intravenous injections of this diplococcus into rabbits.

(3) They had demonstrated diplococci three times in the pia mater from cases of chorea, and once in the brain.

(4) They had demonstrated the diplococcus in the brain and pia mater of the rabbit that had shown the twitching movements.

An account was next given of a remarkable case of meningitis in a boy suffering from rheumatic fever. This boy of rheumatic parentage was admitted to University College Hospital in 1904 suffering, to all appearances, from a very ordinary attack of rheumatic fever, with multiple arthritis, acute dilatation of the heart, and early mitral endocarditis. His recovery under salicylate of sodium treatment was apparently quite a natural one, but nineteen days later, while still convalescent, he developed headache, vomiting, and moderate fever. Later he became unconscious, with convulsive movements of the limbs, and a remarkable temperature of 102·4° in the axilla and groin, and 106·4° in the rectum.

The necropsy showed early healing mitral endocarditis, a little pleurisy, and a severe non-suppurative cerebral and spinal meningitis. A minute diplococcus was present in the exudation in large numbers; it was smaller than the pneumococcus, but showed in some of the films an appearance of capsulation. Experimental inoculations produced at first rapid death in rabbits, and minute capsulated diplococci were present in the blood stream. After two months' culture in an acid medicine, the organism still retained virulence, and produced arthritis. Fully alive to the characters of the pneumococcus, they believed that this was the "diplococcus rheumaticus" in an unusually virulent condition, and thought that this was an example of true rheumatic meningitis. Finally, allusion was made to the investigations of Josué and Salomon, and also of Gandy, upon cases of cerebral hyperpyrexia in rheumatism. These investigations had pointed to that condition as being the result of an acute rheumatic toxæmia. They were led to make the following comparison between rheumatic nervous and rheumatic cardiac lesions. Mild carditis would be comparable to mild chorea, severe pericarditis to rheumatic meningitis, and acute fatal dilatation of the heart to cerebral hyperpyrexia. The paper was illustrated by microscopic slides, showing the diplococcus in the pial tissues.

At a Pathological Meeting held at 11, Chandos Street, on Thursday, December 7, at 8.30 p.m., the following communications were made :—

(43) Dr. John Turner.—*Pathological Anatomy of Idiopathic Epilepsy.*

The theory was advanced that epilepsy is a disease occurring in persons with a defectively developed nervous system associated

with a morbid condition of the blood, whereby it shows a special tendency to intravascular clotting, and that the immediate cause of the fits is sudden stasis of the blood stream, resulting from the blocking of cerebral vessels by these intravascular clots.

The fits are regarded as only a symptom of the general epileptic condition.

Experimental evidence was quoted showing that sudden stasis of blood stream in the brain is capable of setting up convulsions.

In support of this thesis facts were given showing that in nearly all the cases examined appearances pointing to a defective development of the nervous system have been met with, such as:—

(α) A form of nerve-cell showing changes similar to those described as *réaction à distance*.

(β) Persistence of large numbers of subcortical nerve-cells.

Besides these, which may be looked upon as predisposing causes, it is common to meet with an *acute form of cell change* similar to that produced by ligature of the cerebral arteries in a dog.

On the part of the vascular system:—

(α) Large numbers of blood plates.

(β) Different forms of intravascular clotting, probably in large measure derived from amalgamation of the blood plates.

(γ) Small cortical hæmorrhages, which in some cases can be traced to rupture of a vessel blocked up by the aforementioned clot.

(44) Dr. J. Herbert Parsons.—*Brain from a case of orbital meningo-encephalocele.*

The specimen is from a child, aged 5 months, who had right orbital meningo-encephalocele associated with microphthalmia, coloboma of the optic nerve, &c. (see *Trans. Ophthalmological Soc.*, xxv., 1905). The orbit was exenterated, a large mass of brain substance being removed. This mass was found *post mortem* to spring from a large mass lying under the right frontal lobe, which it pressed upwards, and in front of the right temporo-sphenoidal lobe, which it pressed backwards. The mass is covered with pia mater and is attached to the rest of the brain only by the third nerve, which passes through it, and by blood vessels. The brain proper is apparently quite normal, apart from pressure effects. The isolated mass consists of brain substance with definite cortical lamination.

(45) Dr. GORDON HOLMES.—*Specimens from a case of pseudo-hypertrophic paralysis.*

(46) Dr. FRED E. BATTEN.—*Two cases of acute anterior poliomyelitis.*

(47) Dr. LEONARD GUTHRIE.—*Congenital hydrocephalus and cerebellar tumour from a youth who died, aged* 19.

Other specimens were also exhibited.

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EDITOR.

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Rules

AND

LIST OF OFFICE BEARERS AND MEMBERS

OF THE

Neurological Society of the United Kingdom

1905

WITH THE

Annual Report of Council, and Balance Sheet for the Year 1904

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1905

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Neurological Society of the United Kingdom.

REPORT OF THE COUNCIL FOR 1904.

FEBRUARY 16, 1905.

The council has much pleasure in reporting the continued prosperity of the Society, which now numbers 245 members.

The Presidential Address given on February 4 by Dr. Sharkey was fully reported in the Spring Number of "Brain." The abstract of the Proceedings shows the scope and character of the work of the Society during the past year. Three meetings were devoted to the illustration of single subjects in Neurology. All these evenings were unusually well attended.

Dr. Beevor resigns the Treasurership after 10 years' whole-hearted service, and the Council wishes to express to him its thanks for his devotion to the interests of the Society.

The Council also regrets that Dr. Percy Smith can no longer undertake the Editorship of "Brain." He assumed the post at a time when the Journal was heavily in debt. The long expected Index to "Brain" was far from completed, and much thankless toil was thrown upon him before he was able to issue it to the Society in 1902. Within four years, by unceasing care, he has so improved the finances of the Journal that there is now a substantial balance, and money can again be devoted to illustrations.

The Council wishes to express its thanks to the senior Secretary, Dr. Head, who retires after four years of most valuable service rendered to the Society. The Council has nominated Dr. Head as Editor of "Brain."

It is hoped that the prosperity of the Society will continue to increase, and so enable it to maintain the present high reputation of its Journal, "Brain."

Proceedings of the Society during the Year 1904.

February 14.—Dr. S. T. SHARKEY, Inaugural Address, "Hysteria and Neurasthenia."

March 17.—Dr. ALFRED W. CAMPBELL, "Histological studies in cerebral localisation."

April 21.—Clinical Meeting. Subject, "Tremor." Dr. JAMES TAYLOR, "Cases of Tremor." Dr. LEONARD GUTHRIE and Dr. RAYNER BATTEN, "Intention tremors, most marked on right side, associated with paresis of left superior rectus muscle, dilatation and inactivity to light of left pupil, unsteadiness of gait, marked 'Romberg's sign,' and active knee-jerks." Dr. HEAD and Mr. ERIC GARDNER, "Tremor in a case of family spastic paralysis." Dr. HEAD, "Tremor from a lesion, possibly of optic thalamus." Dr. LEONARD WILLIAMS (1), "Case of tremor in boy"; (2), "Generalised tremor associated with tabes"; (3), "Tremor of unusual distribution associated with Parkinson's disease." Dr. GEORGE JOHNSTON, "A case of paralysis agitans with intention tremor." Dr. E. FARQUHAR BUZZARD, "Case of tremor in boy." Dr. WILFRED HARRIS, "Case of familial tremor." Dr. T. GRAINGER STEWART, "Case of tremor."

July 14.—Clinical Meeting. Subject, "Muscular atrophy." (1) *Muscular Atrophy of Spinal Cord Origin.*—Dr. HENRY HEAD, "Widespread muscular wasting of both upper extremities with increased knee-jerks and flexor toe response." Dr. FERRIER (1), "Amyotrophic lateral sclerosis (upper arm type);" (2) "Progressive muscular atrophy (? early tabes dorsalis.") (2), *Peroneal Type.* Dr. HENRY HEAD (1), "A case of peroneal muscular atrophy"; (2), "A case of advanced peroneal atrophy." (3), *Neuritic Type.*—Dr. HENRY HEAD (1), "Muscular wasting from brachial neuritis"; (2), "A case of atrophy of the lower portion of the trapezius." (4), *Anomalous Cases.*—Dr. ORMEROD, "? Early syringomyelia or neuritis." (5), *Syringomyelia.*—Dr. FARQUHAR BUZZARD, "Case of syringomyelia. Dr. WILFRED HARRIS, "Case of syringomyelia."

October 27.—Clinical Meeting. Dr. FERRIER and Mr. BALLANCE, "Case of recovery after operation for cauda equina lesion." Dr. FERRIER and Sir V. HORSLEY, "Case of recovery after operation for tumour of cauda equina." Dr. COLMAN, "Case of myasthenia gravis with prominent bulbar symptoms." Dr. ALBERT WILSON, "Progressive muscular atrophy with arthritic changes." Mr. CHARLES BALLANCE (1), "A case of facial palsy treated by hypoglosso-facial and gustatorio-hypoglossal anastomosis"; (2), "A case of facio-accessory anastomosis for facial palsy, with recovery of dissociated movement." Dr. ALDREN TURNER, "Case of facio-accessory anastomosis." Mr. HAMILTON BALLANCE, "A case of facio-accessory anastomosis for facial palsy." Dr. PURVES STEWART and Mr. LENTHAL CHEATLE, "Case of facio-hypoglossal anastomosis." Mr. CHARLES BALLANCE, "A case of temporo-sphenoidal abscess with loss of the sense of smell." Dr. BEEVOR, "Pseudo-bulbar paralysis from bilateral hemiplegia." Dr. RISIEN RUSSELL, "Case of pseudo-bulbar paralysis (double hemiplegia)."

December 1st.—Pathological Meeting. Dr. DAVID ORR, a discussion on "Lesions of the posterior column of the spinal cord in diseases other than tabes dorsalis."

BALANCE SHEET, 1904.

Dr. NEUROLOGICAL SOCIETY. **Cr.**

RECEIPTS.	£	s.	d.	EXPENDITURE.	£	s.	d.
To Balance	62	0	10	By Messrs. Macmillan for publishing "Brain," 1904	143	8	3
Subscriptions	243	14	6	Stationery and Printing—			
Half-Share profit on "Brain"	50	10	6	Bale and Danielsson £33 17 3			
Contribution of Messrs. Macmillan towards cost of Illustrations for 1904	16	16	10	Pulman 11 0	34	8	3
				Illustrations—Contributors of Papers £49 0 0			
				,, Bale and Danielsson 38 8 3	87	8	3
				Microscopes—Baker and Son	3	5	0
				Lantern—Hawes	1	10	0
				Hire of Rooms and Refreshments—			
				Medical Society	21	15	0
				Petty Cash	2	13	4
				Balance	78	14	7
	£373	2	8		£373	2	8

Account for Publishing Index to "Brain," Vols. I.—XXIII.

	£	s.	d.		£	s.	d.
To Sale of Index (less Commission)	3	15	6	By Messrs. Macmillan on Index Account	54	10	0
Balance against	50	14	6				
	£54	10	0		£54	10	0

General Statement.

	£	s.	d.		£	s.	d.
To Balance on General Account	78	14	7	By Messrs. Macmillan on Index Account	50	14	6
				Balance	28	0	1
	£78	14	7		£78	14	7

Audited and found correct, January 9, 1905 { H. CAMPBELL THOMSON. J. S. COLLIER.

CHARLES E. BEEVOR, *Treasurer.*

RULES.

1.—The Society shall be called the NEUROLOGICAL SOCIETY OF THE UNITED KINGDOM.

2.—The objects of the Society shall be to promote the advance of Neurology and to facilitate intercourse amongst those who cultivate it, whether from a Psychological, Physiological, Anatomical, or Pathological point of view.

3.—The Society shall consist of Ordinary, Corresponding, and Honorary Members.

4.—Any one engaged in researches bearing on Neurology, or manifesting interest in such researches, shall be eligible for the Ordinary Membership.

5.—Men of distinction in Science, who have contributed to the advancement of Neurology, shall be eligible for the Honorary, or for the Corresponding Membership.

6.—The number of Honorary Members shall be limited to six, and that of Corresponding Members to twelve.

7.—Honorary and Corresponding Members shall have the right of attending the Meetings of the Society and of taking part in them.

8.—Honorary and Corresponding Members shall be elected by the Society on the recommendation of the Council.

9.—Candidates for Ordinary Membership shall be recommended by at least three Members of the Society, who shall append their names to a printed form supplied by the Secretaries to any person seeking Membership.

10.—The Council shall nominate candidates for election into the Society as Ordinary Members from among persons so recommended.

11.—The names of Candidates nominated by the Council shall be submitted to the next Meeting of the Society, and shall be balloted for at the next subsequent meeting, one black ball in ten excluding.

12.—The Annual Subscription of an Ordinary Member shall be One Guinea, due in advance.

13.—The Treasurer shall send to each Member, shortly before the Annual General Meeting, a notice reminding him that his Subscription becomes due on that day.

14.—Non-payment of the Subscription within twelve months after it is due shall be considered as equivalent to resignation.

15.—The Council shall consist of a President, two Vice-Presidents, two Secretaries, one Treasurer, the Editor of "Brain," and twelve Councillors, of whom not less than three shall be extra-Metropolitan Members.

16.—Five Members of the Council shall form a quorum.

17.—The office of President shall be tenable for one year, and be entered upon at the beginning of each year by the Senior Vice-President.

18.—The office of Vice-President shall be tenable for two years, one Vice-President being elected every year.

19.—The Secretaries and Treasurer shall be elected annually with eligibility for re-election.

20.—The Councillors shall be elected for one year, and not more than eight shall be eligible for re-election to the same office during the following year.

21.—One full week before the Annual General Meeting, the Secretaries shall send to each Member a balloting paper containing the names of the Officers and Councillors whom the Council nominate for the ensuing year.

22.—The Society shall elect the Council by ballot, each Member, however, being at liberty to substitute other names for any of those upon the list.

23.—There shall be six Ordinary Meetings annually, of which the first held in each year shall be the Annual General Meeting.

24.—Notices of each meeting, and of the subjects to be considered, shall be sent by the Secretaries to each Member of the Society at least one week before the meeting.

25.—Special Meetings shall be held at the option of the Council, or at the request, in writing, of twenty Members.

26.—The President shall have the power of inviting any person to attend and to take part in the scientific work of the meeting.

27.—If at any time the Council shall be of opinion that the interests of the Society require the expulsion of a Member, they shall submit the question to a special General Meeting, at which, if more than one-half of the Members of the Society vote, by ballot as usual, for the expulsion of the Member, his subscription for the current year shall be returned to him, and he shall thereupon cease to be a Member of the Society.

28.—The Council shall draw up and submit for the approval of the Society, supplementary rules regulating the dates, places, and character of the meetings; shall propose special subjects for investigation by the Society, and shall nominate sub-committees for the methodical carrying out of such investigations. They shall decide, from time to time, on the form of publication which its proceedings are to assume.

29.—No alteration shall be made in the present rules, excepting at the Annual Meeting, or at a Special Meeting convened for the purpose, and unless it be proposed by the Council, or in writing by at least twenty Members, the usual notice be given of the proposed change to every Member before the meeting at which it is to be brought forward.

Each Member receives quarterly, from the beginning of the year in which he is elected, a copy of "BRAIN; a Journal of Neurology," the organ of the Society, and edited for it by Henry Head, M.D., F.R.S.

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*** Members are requested to communicate with the Secretaries when corrections are necessary.

—:o:—

EXPLANATION OF ABBREVIATIONS.

O.M., Original Member.	Tr., Treasurer.
Pres., President.	Sec., Secretary.
V.-P., Vice-President.	C., Member of Council.

H.J.L., Hughlings Jackson Lecturer.

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Elected

1899 ABRAHAMS, BERTRAM, M.B., M.R.C.P., 14, Welbeck Street, W.

1897 ANDERSON, H. KERR, M.D., B.Sc., Whitefield, Great Shelford, Cambs.

1894 ANDRIEZEN, W. LLOYD, M.D., 7, Apsley Terrace, Acton, W.

1903 ARMOUR, D. J., M.B., F.R.C.S., 89, Harley Street, W.

1904 ASCHERSON, W. LAWRENCE, M.B., M.R.C.P., St. George's Hospital, W.

1891 BALLANCE, C. A., M.S., F.R.C.S., 106, Harley Street, W. (C., 1897-1900.)

O.M. BARLOW, Sir THOMAS, Bart., K.C.V.O., M.D., F.R.C.P., 10, Wimpole Street, W. (V.-P., 1904-05.)

1902 BARNES, A. STANLEY, M.D., 141, Great Charles Street, Birmingham.

1897 BARRATT, J. O. WAKELIN, M.D., F.R.C.S., Bertheaustrasse 6, Göttingen.

O.M. BASTIAN, H. CHARLTON, M.D., F.R.C.P., F.R.S., 8A, Manchester Square, W. (Pres., 1892; V.-P., 1891; C., 1886-89, 1893-95.)

1897 BATTEN, FREDERICK E., M.D., F.R.C.P., 33, Harley Street, W. (Sec., 1903-05.)

1903 BAYLISS, W. M., M.A., D.Sc., F.R.S., St. Cuthbert's, West Heath Road, Hampstead.

O.M. BEACH, FLETCHER, M.B., F.R.C.P., Winchester House, Kingston Hill, Surrey. (C., 1903-05.)

1903 BEDDARD, A. P., M.D., F.R.C.P., 44, Seymour Street, Portman Square.

O.M. BEEVOR, C. E., M.D., F.R.C.P., 135, Harley Street, W. (Tr., 1894-1905; V.P., 1905; C., 1893.)

1903 BERRY, GEORGE A., M.B., F.R.C.S.Edin., 31, Drumsheugh Gardens, Edinburgh.

1898 BOLTON, JOSEPH SHAW, M.D., B.S., B.Sc., East Sussex County Asylum, Hellingly, S.O., Sussex.

1896 BOND, C. HUBERT, M.D., D.Sc., London County Colony for Epileptics, Ewell, Surrey.

1899 BOND, J. W., M.D., B.S., 26, Harley Street, W.

1892 BOWLBY, ANTHONY A., C.M.G., F.R.C.S., 24, Manchester Square, W.

1898 BOYCE, RUBERT W., M.B., F.R.S., University College, Liverpool.

1889 BRADFORD, J. R., M.D., D.Sc., F.R.C.P., F.R.S., 8, Manchester Square, W.

Elected

O.M. BRAMWELL, BYROM, M.D., F.R.C.P.Ed., 23, Drumsheugh Gardens, Edinburgh. (C., 1894, 1903-05.)

1899 BRAMWELL, EDWIN, M.B., C.M., M.R.C.P., 23, Drumsheugh Gardens, Edinburgh.

1895 BRAMWELL, JOHN MILNE, M.B., C.M., 33, Wimpole Street, W.

1892 BRISTOWE, HUBERT CARPENTER, M.D., Wrington, Somerset.

O.M. BROADBENT, Sir WM. H., Bart., K.C.V.O., M.D., F.R.C.P., F.R.S., 84, Brook Street, W. (Pres., 1895; V.-P., 1893; C., 1886-87, 1896.)

1894 BRODIE, T. GRIGOR, M.D., F.R.S., 4, Lancaster Terrace, N.W.

1897 BROWN, H. H., M.D., F.R.C.S., 22, Museum Street, Ipswich.

1888 BROWN, SANGER, M.D., 100, State Street, Chicago.

O.M. BRUCE, ALEX., M.D., F.R.C.P.Ed., 8, Ainslie Place, Edinburgh. (C., 1895.)

O.M. BRUCE, J. MITCHELL, M.D., F.R.C.P., 23, Harley Street, W.

O.M. BRUNTON, Sir T. LAUDER, M.D., F.R.C.P., F.R.S., 10, Stratford Place, W. (C., 1896-98.)

1895 BRYAN, FREDERICK, M.B., Horton House, Horton, Epsom.

1895 BRYANT, JOHN HENRY, M.D., F.R.C.P., 8, Mansfield Street, Portland Place, W.

1903 BUBB, WILLIAM, M.R.C.S., L.R.C.P., County Asylum, Powick, Worcester.

1890 BURY, JUDSON SYKES, M.D., F.R.C.P., 10, St. John Street, Manchester. (C. 1905.)

1900 BUZZARD, E. FARQUHAR, M.D., M.R.C.P., 33, Harley Street, W.

O.M. BUZZARD, THOMAS, M.D., F.R.C.P., 74, Grosvenor Street, W. (Pres., 1890; V.-P., 1888-89; C., 1886-87, 1891-95.)

1898 CALEY, H. A., M.D., F.R.C.P., 24, Upper Berkeley Street, W.

1903 CAMPBELL, A. W., M.D., County Asylum, Rainhill, Lancs.

1898 CAMPBELL, HARRY, M.D., F.R.C.P., 23, Wimpole Street, W.

1899 CHAMBERS, JAMES, M.A., M.D., The Priory, Roehampton.

1891 CLARKE, J. MICHELL, M.D., F.R.C.P., 28, Pembroke Road, Clifton, Bristol. (C., 1903-05.)

1903 CLOUSTON, T. S., M.D., F.R.C.P.Ed., Royal Asylum, Morningside, Edinburgh.

1892 COLE, ROBERT HENRY, M.D., M.R.C.P., 48, Upper Berkeley Street, Portman Square.

1900 COLE, SYDNEY JOHN, M.O. Wilts County Asylum, Devizes.

1899 COLLIER, J. S., M.D., B.Sc., F.R.C.P., 57A, Wimpole Street, W. (C., 1905.)

1890 COLMAN, W. S., M.D., F.R.C.P., 9, Wimpole Street, W. (Sec., 1899-1902. C., 1903-05.)

1890 CORNER, HARRY, M.D., Brook House, Southgate, Middlesex.

1899 COUPLAND, SIDNEY, M.D., F.R.C.P., 16, Queen Anne Street, W.

1901 COX, JOSHUA JOHN, M.D., St. Ronan's, Clarendon Road, Eccles, Manchester.

1901 CRAIG, MAURICE, M.D., M.R.C.P., Bethlem Royal Hospital, S.E.

1898 DARLEY-HARTLEY, W., M.D., M.R.C.P., Main Road, Sea Point, Cape Town, South Africa.

1895 DAVIDSON, ANDREW, M.D., Callan Park, Sydney, N.S.W.

1897 DAWSON, WILLIAM R., M.D., F.R.C.P.I., Farnham House, Finglas, co. Dublin, Ireland.

Elected

1898 Dodd, Henry Work, F.R.C.S., 136, Harley Street, W.

O.M. Dreschfeld, Julius, M.D., F.R.C.P., Stanley House, Wilmslow Road, Withington, Manchester. (V.-P., 1898-99.)

O.M. Drummond, David, M.D., 6, Saville Place, Newcastle-on-Tyne.

1903 Dudgeon, L. S., M.R.C.P., 6, Powis Gardens, London, W.

1892 Dupuy, Eugene, M.D., 53, Avenue Montaigne, Paris.

1899 Fawcett, John, M.D., F.R.C.P., 66, Wimpole Street, W.

O.M. Ferrier, David, M.D., F.R.C.P., F.R.S., 34, Cavendish Square, W. (Pres., 1886; V.-P., 1892-3; C., 1886, 1890-95.)

1903 Flashman, J. F., M.B., Ch.M., B.Sc., Totnes, Temple Street, Petersham, Sydney, Australia.

1903 Fleming, Robert, M.D., F.R.C.P.Ed., 10, Chester Street, Edinburgh.

1903 Fletcher, H. Morley, M.D., F.R.C.P., 98, Harley Street, W.

O.M. Gaskell, W. H., M.D., F.R.S., The Uplands, Great Shelford, Cambs. (Pres., 1899; V.-P., 1897-98; C., 1896, 1900.)

1903 Gibson, G. A., M.D., D.Sc., F.R.C.P.Ed., 3, Drumsheugh Gardens, Edinburgh.

1904 Giglioli Guiolo T., M.D., M.R.C.P., Via Farinata Degli Ulorti, 4, Florence.

O.M. Godlee, R. J., M.B., F.R.C.S., 19, Wimpole Street, W.

1902 Goldschmidt, Oscar Bernard, M.B., Bishopstone House, Bedford.

1899 Goodall, Edwin, M.D., F.R.C.P., Joint Counties Asylum, Carmarthen.

1897 Gossage, Alfred Milne, M.B., F.R.C.P., 54, Upper Berkeley Street, W.

1892 Gotch, Francis, M.A., F.R.S., The Lawn, Banbury Road, Oxford.

1893 Grant, J. Dundas, M.D., F.R.C.S., 18, Cavendish Square, W.

O.M. Gunn, R. Marcus, M.B., F.R.C.S., 54, Queen Anne Street, W. (C., 1899-1900.)

1895 Guthrie, Leonard, M.D., F.R.C.P., 15, Upper Berkeley Street, W. (C., 1904; Sec. 1905.)

1902 Hall, W. Hamilton, M.R.C.S., Fordcombe, Tunbridge Wells.

1893 Halliburton, William Dobinson, M.D., F.R.C.P., F.R.S., Church Cottage, 17, Marylebone Road, N.W.

O.M. Hamilton, D. J., M.B., F.R.S.E., University, Aberdeen.

1898 Hanbury, William R., M.R.C.S., L.R.C.P., West Ham Borough Asylum, Goodmayes, Ilford.

1904 Harris, David, F., M.D., The University, St. Andrews.

1897 Harris, Wilfred J., M.D., M.R.C.P., 37, Queen Anne Street, W.

1898 Haslett, John Hanfield, M.R.C.S., L.R.C.P., Halliford House, Sunbury-on-Thames.

1891 Hawkins, Herbert Pennell, M.D., F.R.C.P., 56, Portland Place, W.

O.M. Haycraft, J. B., M.D., D.Sc., F.R.S.E., University College of South Wales, Cardiff.

1891 Head, Henry, M.D., F.R.C.P., F.R.S., 143, Harley Street, W. (C., 1900; Sec., 1901-1904; Editor of "Brain," 1905.)

O.M. Hill, Alex., M.A., M.D., Downing Lodge, Cambridge. (Pres., 1896; V.-P., 1895; C., 1892-94.)

1905 Hobhouse, Edmund, M.D., F.R.C.P., 12, Second Avenue, Brighton (Hove).

Elected

1903 HOLMES, GORDON M., M.B., B.Ch., National Hospital, Queen Square, W.C.

O.M. HORSLEY, Sir VICTOR, F.R.C.S., F.R.S., 25, Cavendish Square, W. (Pres., 1898; V.-P., 1896-97; C., 1892-93, 1899.)

1903 HOWLAND, GOLDWIN, W., M.B., M.R.C.P., c/o Dr. Sheraton, Wycliff College, Toronto, Canada.

1889 HUGGARD, WILLIAM R., M.D., F.R.C.P., Davoz Platz, Switzerland.

1896 HULME, GEORGE FREDERICK, M.B., C.M., South View, Montague Road, Felixstowe.

1904 HUMPHREYS, F. R., M.R.C.S., L.R.C.P., 27, Fellows Road, South Hampstead.

1889 HUMPHRY, LAURENCE, M.D., F.R.C.P., Lensfield, Cambridge.

1903 HUNTER, WALTER K., M.D., D.Sc., 7, Woodside Place, Glasgow.

1901 HUNTER, WILLIAM, M.B., C.M., Government Bacteriological Laboratory, Hong Kong.

1903 HUNTER, WILLIAM, M.D., F.R.C.P., 103, Harley Street, W.

O.M. HUTCHINSON, JONATHAN, F.R.C.S., F.R.S., 15, Cavendish Square, W. (Pres., 1889; V.-P., 1887-88; C., 1886, 1890.)

1889 HYSLOP, T. B., M.D., C.M., Bethlem Royal Hospital, Lambeth, S.E.

O.M. JACKSON, J. HUGHLINGS, M.D., F.R.C.P., F.R.S., 3, Manchester Square, W. (Pres., 1886; H.J.L., 1897; C., 1887, 1892.). Hon. Memb., 1904.

O.M. JESSOP, W. H., M.B., F.R.C.S., 73, Harley Street, W.

1895 JOHNSTON, GEORGE, M.D., M.R.C.P., 3, Montagu Place, Montagu Square, W.

1903 JONES, A. E., M.B., B.Sc., University College Hospital, Gower Street.

1892 JONES, HENRY LEWIS, M.D., F.R.C.P., 143, Harley Street, W.

1894 JONES, ROBERT, M.D., F.R.C.S., Claybury Asylum, Woodford, Essex.

1904 JONES, ROBERT, F.R.C.S.Ed., 11, Nelson Street, Liverpool.

1902 KELYNACK, T. N., M.D., M.R.C.P., 120, Harley Street, W.

1894 KIDD, PERCY, M.D., F.R.C.P., 60, Brook Street, W. (C., 1904.)

1896 LANGDON, F. W., M.D., Cincinnati, Ohio, U.S.A.

1898 LANGDON-DOWN, REGINALD L., M.B., M.R.C.P., 47, Welbeck Street, W.

O.M. LANGLEY, J. N., M.A., D.Sc., F.R.S., Hedgerley Lodge, Madingley Road, Cambridge. (Pres., 1903; V.-P., 1901-1902; C., 1898-99, 1904.)

1888 LAWFORD, J. B., M.D., F.R.C.S., 99, Harley Street, W. (C., 1902-3.)

O.M. LEES, D. B., M.D., F.R.C.P., 22, Weymouth Street, W. (C., 1901-1903.)

1897 LEWIS, H. WOLSELEY, M.R.C.S., L.R.C.P., London County Asylum, Banstead, Surrey.

1904 LINDSAY, J. A., M.D., F.R.C.P., 13, College Square E., Belfast.

1897 LOEWENTHAL, MAX, M.D., M.R.C.P., 126, Princes' Road, Liverpool.

1899 LORD, JOHN R., M.B., C.M., London County Asylum, Bexley, Kent.

1898 MCALDOWIE, ALEXANDER M., M.D., 6, Brook Street, Stoke-on-Trent.

1898 MACCORMAC, JOHN M'GEE, M.D., 73, Victoria Place, Belfast.

1891 MACDONALD, PETER WILLIAM, M.D., C.M., The County Asylum, Dorchester, Dorset.

Elected

1902 McDOUGALL, WM., M.B., Weald Mount, Haslemere.

1902 MACKENZIE, JAMES, M.D., Bank Parade, Burnley.

O.M. MACKENZIE, Sir STEPHEN, M.D., F.R.C.P., 31, Cavendish Square, W. (C., 1896-98.)

1896 MACKINTOSH, ASHLEY W., M.A., M.D., 9, Bon Accord Square, Aberdeen.

1903 MACNAMARA, E. D., M.B., B.C., 45, Campden House Road, W.

O.M. MAGUIRE, ROBERT, M.D., F.R.C.P., 4, Seymour Street, W. (Sec., 1890-93; C., 1893-96.)

O.M. MANN, J. DIXON, M.D., F.R.C.P., 16, St. John Street, Manchester.

1902 MANTLE, ALFRED, M.D., M.R.C.P., Savile Place, Halifax.

1901 MARRIS, W. A., M.D., Springfield Road, King's Heath, Birmingham.

1894 MARTIN, SIDNEY, M.D., F.R.C.P., F.R.S., 10, Mansfield Street, W.

1891 MAY, W. PAGE, M.D., F.R.C.P., 9, Manchester Square, W.

1890 MENZIES, WILLIAM FRANCIS, M.D., B.Sc., M.R.C.P., Cheddleton Asylum, Leek, Staffordshire.

O.M. MERCIER, C., M.B., F.R.C.P., Flower House, Southend, Catford, S.E. (C., 1899-1902.)

1897 MEYER, ADOLF, M.D., LL.D., Pathological Institute, New York State Hospital, Ward's Island, N.Y., U.S.A.

O.M. MICKLE, W. JULIUS, M.D., F.R.C.P., Grove Hall Asylum, Bow, E. (Pres., 1901; V.-P., 1900; C., 1895-97, 1902-4.)

1905 MILNE, ROBERTSON CHAS. JOHN, I.M.S., M.B., C.M., c/o Inspector General of Civil Hospitals, Bengal, Calcutta.

1895 MOORE, NORMAN, M.D., F.R.C.P., 94, Gloucester Place, W.

O.M. MORRIS, MALCOLM, F.R.C.S.Ed., 8, Harley Street, W.

1902 MORRISON, C. S., L.R.C.P.E., County and City Asylum, Hereford.

1888 MOTT, F. W., M.D., F.R.C.P., F.R.S., 25, Nottingham Place, W. (Sec., 1894-98; C., 1899-1902.)

1901 MOULD, GEORGE WM., M.R.C.S., Cheadle Royal Asylum, Manchester.

1899 MOULD, GILBERT E., M.R.C.S., L.R.C.P., The Grange, nr. Rotherham.

1894 MURRAY, GEORGE R., M.A., M.D., F.R.C.P., 11, Ellison Place, Newcastle-on-Tyne.

1889 MURRAY, H. MONTAGUE, M.D., F.R.C.P., 25, Manchester Square, W.

1904 MYERS, CHARLES S., M.D., Melrose, Grange Road, Cambridge.

1904 NEILD, NEWMAN, M.D., Richmond Hill, Clifton, Bristol.

O.M. NETTLESHIP, EDWARD, F.R.C.S., Shottermill, Haslemere, Surrey.

1902 NEWINGTON, HAYES, F.R.C.P.Ed., The Gables, Ticehurst, Sussex.

O.M. NICOLSON, DAVID, C.B., M.D., M.R.C.P.Ed., Balgownie, Guildford, Surrey.

1888 NIERMEYER, J. H. H., M.D., Amsterdam.

1904 NOLAN, M. J., L.R.C.P., L.R.C.S.I., Down District Asylum, Downpatrick.

1888 NORMAN, CONOLLY, F.R.C.P.I., F.R.C.S.I., St. Dymphna's, N. Circular Road, Dublin.

1887 OGILVIE, GEORGE, M.B., M.R.C.P., 22, Welbeck Street, W.

1887 OLIVER, THOMAS, M.D., F.R.C.P., 7, Ellison Place, Newcastle-on-Tyne.

O.M. ORANGE, WM., C.B., M.D., F.R.C.P., Oakhurst, Godalming, Surrey.

O.M. ORMEROD, J. A., M.D., F.R.C.P., 25, Upper Wimpole Street, W. (C., 1895-97.)

Elected

1899 ORR, DAVID, M.D., County Asylum, Prestwich, Manchester.

1904 OWEN, ARTHUR GEOFFRY, M.D., B.Sc., c/o Prof. Marich, Chanoury University, Melbourne.

O.M. PAGE, HERBERT WILLIAM, M.A., F.R.C.S., 146, Harley Street, W. (Pres., 1902; V.-P., 1900-1; C., 1891-92, 1903-05.)

1903 PALMER, FREDK. S., M.D., M.R.C.P., 19, Harley Street, W.

1895 PARKINSON, JOHN PORTER, M.D., M.R.C.P., 57, Wimpole Street, W.

1901 PARSONS, JOHN HERBERT, D.Sc., F.R.C.S., 27, Wimpole Street, W.

1901 PASSMORE, E. S., M.D., M.R.C.P., Croydon Asylum, Warlingham, Surrey.

1896 PATERSON, DONALD ROSE, M.D., M.R.C.P., 15, St. Andrew's Crescent, Cardiff.

1904 PATON, LESLIE, J., M.B., F.R.C.S., 1, Spanish Place, W.

1899 PIPER, FRANCIS P., M.B., M.R.C.S., L.R.C.P., King's Leigh, Tankerton, Whitstable.

1888 PITT, G. N., M.D., F.R.C.P., 15, Portland Place, W. (C., 1903-05).

1899 RAMBAUT, DANIEL F., M.D., B.Ch., County Asylum, Bicton Heath, Shrewsbury.

1894 RANSOM, WILLIAM B., M.D., F.R.C.P., The Pavement, Nottingham.

1890 RAYNER, HENRY, M.D., M.R.C.P.Ed., 16, Queen Anne Street, W.

O.M. REID, E. W., M.B., F.R.S., University College, Dundee.

1897 REISSMANN, CHARLES H., M.B., B.Sc., St. Peter's, Adelaide, South Australia.

1893 RENNIE, GEORGE E., M.D., M.R.C.P., College Street, Sydney.

1895 REYNOLDS, ERNEST S., M.D., F.R.C.P., 2, St. Peter's Square, Manchester.

1891 RIVERS, W. H. R., M.A., M.D., F.R.C.P., St. John's College, Cambridge. (C., 1897-98.)

1898 ROBERTSON, WILLIAM FORD, M.D., 7, Hill Square, Edinburgh.

1892 ROWE, EDMUND LEWIS, L.R.C.P., L.R.C.S., Borough Asylum, Ipswich.

1901 ROWS, R. G., M.D., County Lunatic Asylum, Lancaster.

1892 RUFFER, MARC ARMAND, M.D., Ramleh, Egypt.

1903 RUSSELL, A. E., M.D., M.R.C.P., 9, Wimpole Street, W.

1889 RUSSELL, J. S. RISIEN, M.D., F.R.C.P., 44, Wimpole Street, W. (Sec., 1896-1900; C., 1901-1904.)

1899 RUSSELL, J. W., M.D., M.R.C.P., 72, Newhall Street, Birmingham.

1901 SALAMAN, REDCLIFFE N., M.A., M.B., Frognal End, Frognal Gardens, Hampstead.

O.M. SANDERSON, Sir J. BURDON, Bart., M.D., F.R.C.P., F.R.S., Banbury Road, Oxford.

O.M. SAVAGE, G. H., M.D., F.R.C.P., 3, Henrietta Street, Cavendish Square. (Pres., 1897; V.-P., 1895; C., 1886-90, 1898.)

1888 SAVILL, T. D., M.D., M.R.C.P., 60, Upper Berkeley Street, W.

O.M. SCHÄFER, E. A., F.R.S., University of Edinburgh. (Pres., 1893; V.-P., 1892; C., 1886-98.)

1901 SCHORSTEIN, GUSTAVE, M.D., F.R.C.P., 11, Portland Place, W.

O.M. SEMON, Sir FELIX, C.V.O., M.D., F.R.C.P., 39, Wimpole Street, W. (C., 1899-1901.)

1898 SEWARD, WM. JOSEPH, M.B., Colney Hatch Asylum, N.

Elected

O.M. SHARKEY, S. J., M.D., F.R.C.P., 22, Harley Street, W. (Pres., 1904; V.-P., 1902-3; C., 1899-92, 1905.)

O.M. SHERRINGTON, C. S., M.D., F.R.S., 16, Grove Park, Liverpool. (C., 1892-95.)

1894 SHUTTLEWORTH, GEORGE E., M.D., Ancaster House, Richmond.

1900 SINGER, H. D., M.D., M.R.C.P., Maccagne Buildings, Omaha, Neb., U.S.A.

1895 SMITH, F. J., M.D., F.R.C.P., 138, Harley Street, W.

1887 SMITH, R. PERCY, M.D., F.R.C.P., 36, Queen Anne Street, W. (Editor of "Brain," 1901-1904; C. 1905.)

1895 SPICER, W. T. HOLMES, M.B., F.R.C.S., 5, Wimpole Street, W.

1901 STAFFORD, WILLIAM, M.B., 110, Mansfield Road, Nottingham.

1895 STANLEY, DOUGLAS, M.D., M.R.C.P., 21, Broad Street, Birmingham.

1895 STANSFIELD, THOS. E. K., M.B., London County Asylum, Bexley, Kent.

1892 STARLING, ERNEST HENRY, M.D., F.R.C.P., F.R.S., 40, West End Lane, Hampstead (C., 1904-05.)

1901 STEELL, GRAHAM, M.D., F.R.C.P., 96, Mosley Street, Manchester.

1897 STEWART, PURVES, M.A., M.D., M.R.C.P., 7, Harley Street, W.

1903 STEWART, T. GRAINGER, M.B., B.Ch., M.R.C.P., National Hospital, Queen Square, W.C.

1897 STIRLING, WM., M.D., D.Sc., Owens College, Manchester.

1897 STODDART, WM. H., M.D., M.R.C.P., Bethlem Royal Hospital, Lambeth, S.E.

1902 STONE, W. G., M.D., 93, Denmark Hill, S.E.

1902 SULLIVAN, WM. CHARLES, M.D., H.M. Prison, Pentonville, N.

1904 SUTHERLAND, GEO. ALEXANDER, M.D., F.R.C.P., 73, Wimpole Street, W.

1888 SYERS, HENRY W., M.D., M.R.C.P., 75, Wimpole Street, W.

1898 TAYLOR, F. R. P., M.D., East Sussex Asylum, Hellingly, Sussex.

1891 TAYLOR, JAMES, M.D., F.R.C.P., 49, Welbeck Street, W. (C., 1900-3 Tr., 1905.)

1898 THOMSON, H. CAMPBELL, M.D., F.R.C.P., 34, Queen Anne Street, W.

1889 THORBURN, WM., F.R.C.S., Oxford Lodge, Victoria Park, Manchester. (C., 1901-1903.)

1892 TITCHENER, E. B., B.A., Ph.D., Cornell Heights, Ithaca, N.Y.

O.M. TOOTH, H. H., C.M.G., M.D., F.R.C.P., 34, Harley Street, W. (Sec., 1891-95; C., 1896-99.)

1892 TREVELYAN, E. F., M.D., B.Sc., F.R.C.P., 40, Park Square, Leeds.

1892 TUCKEY, CHARLES LLOYD, M.D., 88, Park Street, Grosvenor Square, W.

1892 TUKE, Sir J. BATTY, M.D., F.R.C.P.Ed., F.R.S.Ed., 20, Charlotte Square, Edinburgh. (V.P., 1903-04; Pres., 1905.)

1891 TUKE, THOMAS SEYMOUR, M.B., Chiswick House, Chiswick.

1891 TURNER, WILLIAM ALDREN, M.D., F.R.C.P., 18, Harley Street.

1898 TURNEY, HORACE G., M.D., F.R.C.P., 68, Portland Place, W.

O.M. TWEEDY, JOHN, F.R.C.S., 100, Harley Street, W.

1901 VINCENT, SWALE, M.B., Physiological Laboratory, University of Manitoba, Winnipeg, Canada.

1888 VOORTHUS, J. A., M.D., Apeldoorn, 542, Loulaan, Netherlands.

Elected

O.M. WALLER, AUGUSTUS, M.D., F.R.S., 32, Grove End Road, N.W. (Pres., 1900; V.-P., 1899; C., 1894-97, 1901.)

O.M. WARNER, FRANCIS, M.D., F.R.C.P., 5, Prince of Wales Terrace, Kensington Palace, W.

1902 WARRINGTON, W. B., M.D., M.R.C.P., 69, Rodney Street, Liverpool.

1904 WATSON, CHALMERS, M.B., F.R.C.P.E., 22, Coates Crescent, Edinburgh.

O.M. WATTEVILLE, A. DE, M.A., M.D., B.Sc., 30, Welbeck Street, W. (C., 1890-95, 1896-1902; Sec., 1886-89; Editor of "Brain," 1880-1900.)

1897 WEBER, F. PARKES, M.D., F.R.C.P., 19, Harley Street, W.

1897 WEST, SAMUEL, M.D., F.R.C.P., 15, Wimpole Street, W.

1897 WHITE, ERNEST W., M.B., M.R.C.P., City of London Asylum, Dartford.

O.M. WHITE, W. HALE, M.D., F.R.C.P., 65, Harley St., W. (C., 1897-1902.)

1894 WHITING, ARTHUR J., M.D., M.R.C.P., 142, Harley Street, W.

1889 WIGLESWORTH, JOSEPH, M.D., F.R.C.P., County Asylum, Rainhill, Lancashire.

1905 WILKIN, GRIFFITH CHARLES, M.R.C.S., L.R.C.P.Lond., Conway House, Paignton, Devon.

1900 WILLIAMS, LEONARD, M.D., M.R.C.P., 8, York Street, Portman Square, W.

1894 WILLIAMSON, RICHARD T., M.D., F.R.C.P., 2, St. Peter's Square, Manchester.

1896 WILSON, ALBERT, M.D., 1, Belsize Park, N.W.

1903 WILSON, G. R., M.D., M.R.C.P.Ed., 8, Rutland Square, Edinburgh.

1905 WILSON, S. A. K., M.A., M.B., Ch.B., B.Sc., National Hospital, Queen Square, Bloomsbury.

1896 WOOD, GUY M., M.B., 49, Gordon Square, W.C.

1889 WOOD, T. OUTTERSON, M.D., F.R.C.P.Ed., 40, Margaret Street, Cavendish Square, W.

1892 WOODHEAD, G. SIMS, M.D., F.R.C.P.Ed., 6, Scroope Terrace, Cambridge.

1899 WRIGHT, HAMILTON, M.D., Pathological Institute, Selangor, Straits Settlement.

1898 YOUNG, ROBERT ARTHUR, M.D., B.Sc., M.R.C.P., 41, Wimpole St., W.

The Neurological Society of the United Kingdom.

ABSTRACT of a Paper upon "Some Investigations on Acute Rheumatic Nervous Affections," by Dr. POYNTON and Dr. ALEXANDER PAINE, to be read at 11, Chandos Street, Cavendish Square, on Thursday, November 23, at 8.30 p.m.

THE paper consisted of three parts. In the first, as a wish had been expressed that the entire question of the etiology of rheumatism should be open to discussion, the writers put forward again their claim that they had proved that a diplococcus was a cause of rheumatic fever, and maintained that it was probably the only bacterial cause of a specific disease. They admitted that some did not believe that rheumatic fever was due to an infection, and held that these should demonstrate a non-bacterial cause, and also explain away the many facts connected with diplococcus which the authors, among others, had found in no less than thirty-two cases. On the other hand, those who maintained that there was more than one bacterial cause of this disease ought, in their opinion, to satisfy Koch's postulates for at least one other micro-organism. So far as they were aware, these had only been demonstrated with the diplococcus.

Lastly, some maintained that rheumatic fever was an infective disease, but that the infection was as yet unknown; they, in response, criticised the objections to the acceptance of the "diplococcus rheumaticus," and held that these objections did not hold good. Although the name "diplococcus rheumaticus" had been cavilled at, the writers were still of the opinion that it was the most accurate and reasonable name.

The second part of the paper was concerned with rheumatic chorea. A brief history was given of the discovery by various

investigators of a diplococcus in the cerebro-spinal fluid and pia mater in rheumatic chorea. Drs. Poynton and Paine had isolated it from the cerebro-spinal fluid in four cases of rheumatic fever fatal with pericarditis, and in two of these cases there had been chorea at the time of death. Two of these they had already published, and they added two more in this contribution. These two cases furnished some additional links to the chain of evidence in favour of rheumatic fever being the result of a local invasion by the "diplococcus rheumaticus."

They had isolated the diplococcus, and had produced, in addition to *arthritis*, which had been produced by Wassermann under similar circumstances in 1899, *pericarditis* and *endocarditis*. They had also demonstrated the micro-organism in the pia mater in both these cases.

Allusion was made to the choreiform movements they had noticed in 1900, produced by intravenous inoculation of the diplococcus into a rabbit, and to a like experience by Meyer in 1902, and Beattie in 1904.

Their present opinion was that rheumatic chorea resulted from multiple local infections of the nervous system rather than from a general blood poisoning, and in support of this some evidence was brought forward.

The third part of the paper was devoted to an account of a remarkable case of meningitis in a boy suffering from rheumatic fever. This boy of rheumatic parentage was admitted to University College Hospital in 1904 suffering, to all appearances, from a very ordinary attack of rheumatic fever, with multiple arthritis, acute dilatation of the heart, and early mitral endocarditis. His recovery under salicylate of sodium treatment was apparently quite a natural one, but nineteen days later, while still convalescent, he developed headache, vomiting, and moderate fever. Later he became unconscious, with convulsive movements of the limbs, and a remarkable temperature of 102·4° in the axilla and groin, and 106·4° in the rectum.

The necropsy showed early healing mitral endocarditis, a little pleurisy, and a severe non-suppurative cerebral and spinal meningitis. A minute diplococcus was present in the exudation in large numbers, and the fibres from these exudations were shown. Experiment caused rapid death in rabbits, and later arthritis was produced. The authors put the case on record as probably one of true rheumatic meningitis.

Lastly, after an allusion to rheumatic hyperpyrexia, they drew

a comparison between rheumatic heart disease and rheumatic nervous disease.

Compare :—

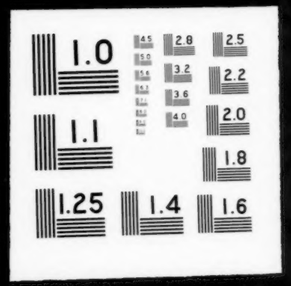
(1) Slight carditis to slight chorea.

(2) Severe pericarditis to rheumatic meningitis.

(3) Acute fatal dilatation of the heart to fatal cerebral hyperpyrexia.

The paper was illustrated by macroscopic and microscopic specimens, drawings, and lantern slides.

RESOLUTION CHART



100 MILLIMETERS

INSTRUCTIONS Resolution is expressed in terms of the lines per millimeter recorded by a particular film under specified conditions. Numerals in chart indicate the number of lines per millimeter in adjacent "T-shaped" groupings.

In microfilming, it is necessary to determine the reduction ratio and multiply the number of lines in the chart by this value to find the number of lines recorded by the film. As an aid in determining the reduction ratio, the line above is 100 millimeters in length. Measuring this line in the film image and dividing the length into 100 gives the reduction ratio. Example: the line is 20 mm. long in the film image, and $100/20 = 5$.

Examine "T-shaped" line groupings in the film with microscope, and note the number adjacent to finest lines recorded sharply and distinctly. Multiply this number by the reduction factor to obtain resolving power in lines per millimeter. Example: 7.9 group of lines is clearly recorded while lines in the 10.0 group are not distinctly separated. Reduction ratio is 5, and $7.9 \times 5 = 39.5$ lines per millimeter recorded satisfactorily. $10.0 \times 5 = 50$ lines per millimeter which are not recorded satisfactorily. Under the particular conditions, maximum resolution is between 39.5 and 50 lines per millimeter.

Resolution, as measured on the film, is a test of the entire photographic system, including lens, exposure, processing, and other factors. These rarely utilize maximum resolution of the film. Vibrations during exposure, lack of critical focus, and exposures yielding very dense negatives are to be avoided.